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predefined hit display formats
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NEWS 5 APR 28 IMSRESEARCH reloaded with enhancements
NEWS 6 MAY 30 INPAFAMDB now available on STN for patent family
searching
NEWS 7 MAY 30 DGENE, PCTGEN, and USGENE enhanced with new homology
sequence search option
NEWS 8 JUN 06 EPFULL enhanced with 260,000 English abstracts
NEWS 9 JUN 06 KOREAPAT updated with 41,000 documents
NEWS 10 JUN 13 USPATFULL and USPAT2 updated with 11-character
patent numbers for U.S. applications
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reclassification data
NEWS 13 JUN 30 AEROSPACE enhanced with more than 1 million U.S.
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NEWS 16 JUN 30 STN AnaVist enhanced with database content from EPFULL
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NEWS 19 JUL 28 IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
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NEWS 21 AUG 01 INPADOCDB and INPAFAMDB coverage enhanced
NEWS 22 AUG 13 CA/CAPLUS enhanced with printed Chemical Abstracts
page images from 1967-1998
NEWS 23 AUG 15 CAOLD to be discontinued on December 31, 2008
NEWS 24 AUG 15 CAPLUS currency for Korean patents enhanced
NEWS 25 AUG 25 CA/CAPLUS, CASREACT, and IFI and USPAT databases
enhanced for more flexible patent number searching
NEWS 26 AUG 27 CAS definition of basic patents expanded to ensure
comprehensive access to substance and sequence
information
NEWS 27 SEP 18 Support for STN Express, Versions 6.01 and earlier,
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AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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=> S sirna (S) NIK AND pd<=20041130
1 FILES SEARCHED...
L1 0 SIRNA (S) NIK AND PD<=20041130

=> S RNA (S) NIK AND pd<=20041130
1 FILES SEARCHED...
L2 17 RNA (S) NIK AND PD<=20041130

=> DUP REM L2
PROCESSING COMPLETED FOR L2
L3 9 DUP REM L2 (8 DUPLICATES REMOVED)
ANSWERS '1-4' FROM FILE MEDLINE
ANSWER '5' FROM FILE BIOSIS
ANSWERS '6-9' FROM FILE CAPLUS

=> D IBIB abs L31-9
'L999-998' IS NOT A VALID FORMAT
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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):L#
'L#' IS NOT A VALID FORMAT
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individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):L3

'L11' IS NOT A VALID FORMAT

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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ibib abs L3 1-9

'L11' IS NOT A VALID FORMAT

'1-9' IS NOT A VALID FORMAT

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REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):T1

L3 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
T1 Genetic evidence for the essential role of beta-transducin repeat-containing protein in the inducible processing of NF-kappa B2/p100.

=> D IBib Abs L3 1-9

L3 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002325290 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11994270
TITLE: Genetic evidence for the essential role of beta-transducin repeat-containing protein in the inducible processing of NF-kappa B2/p100.
AUTHOR: Fong Abraham; Sun Shao-Cong
CORPORATE SOURCE: Department of Microbiology and Immunology, Pennsylvania State University College of Medicine, Hershey, Pennsylvania 17033, USA.
CONTRACT NUMBER: 1R01 AI45045 (United States NIAID)
SOURCE: The Journal of biological chemistry, (2002 Jun 21) Vol. 277, No. 25, pp. 22111-4. Electronic Publication: 2002-05-06.
JOURNAL CODE: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 18 Jun 2002
Last Updated on STN: 5 Jan 2003
Entered Medline: 19 Jul 2002

AB Processing of the nf kappa b2 gene product p100 to generate p52 is an important step in NF-kappa B regulation. This step is regulated by a nonclassical NF-kappa B signaling pathway involving the NF-kappa B-inducing kinase (NIK). NIK induces p100 processing by triggering phosphorylation of specific C-terminal serines of p100. However, the downstream molecular events leading to p100 processing remain unclear. Here we show that NIK induced the physical recruitment of beta-transducin repeat-containing protein (beta-TrCP), a component of the SCF ubiquitin ligase complex, to p100. This event required the phosphorylation sites as well as the death domain of p100. Using the RNA interference technique, we demonstrated that beta-TrCP is essential for NIK-induced p100 ubiquitination and processing. Interestingly the constitutive processing of p100 mutants was independent of beta-TrCP. These results suggest that beta-TrCP is an essential component of NIK-induced p100 processing.

L3 ANSWER 2 OF 9 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2002179110 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11911360
 TITLE: Highly conserved NIKS tetrapeptide is functionally essential in eukaryotic translation termination factor eRF1.
 AUTHOR: Frolova Ludmila; Seit-Nebi Alim; Kisselev Lev
 CORPORATE SOURCE: Engelhardt Institute of Molecular Biology, Moscow, Russia.
 SOURCE: RNA (New York, N.Y.), (2002 Feb) Vol. 8, No. 2, pp. 129-36.
 Journal code: 9509184. ISSN: 1355-8382.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200204
 ENTRY DATE: Entered STN: 26 Mar 2002
 Last Updated on STN: 19 Apr 2002
 Entered Medline: 18 Apr 2002
 AB Class-1 polypeptide chain release factors (RFs) play a key role in translation termination. Eukaryotic (eRF1) and archaeal class-1 RFs possess a highly conserved Asn-Ile-Lys-Ser (NIKS) tetrapeptide located at the N-terminal domain of human eRF1. In the three-dimensional structure, NIKS forms a loop between helices. The universal occurrence and exposed nature of this motif provoke the appearance of hypotheses postulating an essential role of this tetrapeptide in stop codon recognition and ribosome binding. To approach this problem experimentally, site-directed mutagenesis of the NIKS (positions 61-64) in human eRF1 and adjacent amino acids has been applied followed by determination of release activity and ribosome-binding capacity of mutants. Substitutions of Asn61 and Ile62 residues of the NIKS cause a decrease in the ability of eRF1 mutants to promote termination reaction in vitro, but to a different extent depending on the stop codon specificity, position, and nature of the substituting residues. This observation points to a possibility that Asn-Ile dipeptide modulates the specific recognition of the stop codons by eRF1. Some replacements at positions 60, 63, and 64 cause a negligible (if any) effect in contrast to what has been deduced from some current hypotheses predicting the structure of the termination codon recognition site in eRF1. Reduction in ribosome binding revealed for Ile62, Ser64, Arg65, and Arg68 mutants argues in favor of the essential role played by the right part of the NIKS loop in interaction with the ribosome, most probably with ribosomal RNA.

L3 ANSWER 3 OF 9 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 2001225756 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11160844
 TITLE: The NF-kappaB pathway in human endometrium and first trimester decidua.
 AUTHOR: King A E; Critchley H O; Kelly R W
 CORPORATE SOURCE: MRC Human Reproductive Sciences Unit, Centre for Reproductive Biology, 37 Chalmers Street, Edinburgh, EH3 9ET, UK.. A.E.King-1@sms.ed.ac.uk
 SOURCE: Molecular human reproduction, (2001 Feb) Vol. 7, No. 2, pp. 175-83.
 Journal code: 9513710. ISSN: 1360-9947.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200104

ENTRY DATE: Entered STN: 2 May 2001
 Last Updated on STN: 19 Sep 2002
 Entered Medline: 26 Apr 2001

AB Nuclear factor kappa B (NF-kappaB) regulates proinflammatory genes and may be involved in inflammation associated with reproductive events e.g. menstruation, implantation. Activation of NF-kappaB involves several protein kinases and subsequent degradation of an endogenous inhibitor, IkappaBalpha. This study details expression of NF-kappaB pathway intermediates in human endometrium and first trimester decidua. Messenger RNA was detected for IkappaBalpha, and IkappaB kinase gamma (IKKgamma, a scaffolding protein) and the protein kinases, IKKalpha, IKKbeta, NF-kappaB inducing kinase (NIK), mitogen-activated protein kinase Erk kinase kinase 1 (MEKK1) and TANK-binding kinase 1 (TBK1) using real-time quantitative polymerase chain reaction (PCR). IkappaBalpha and TBK1 mRNA were increased in the perimenstrual phase of the menstrual cycle. This suggests that there is activation of NF-kappaB due to premenstrual progesterone withdrawal, since NF-kappaB activity increases IkappaBalpha gene expression. Differential expression of NF-kappaB pathway intermediates occurred when progesterone concentrations increased in early pregnancy; IKKalpha and NIK mRNA levels increased in decidua whilst IKKbeta and MEKK1 mRNA levels declined. Expression profiles of IKKalpha and NIK proteins were determined immunohistochemically. Both were detected in glandular epithelium and endothelium of endometrium. In decidua, both were present in epithelium and decidualized stromal cells. The results of this study suggest that NF-kappaB is activated during menstruation. During early pregnancy, NF-kappaB may also be activated (via IKKalpha-NIK) and may regulate the expression of molecules vital for implantation and successful pregnancy. However, pro-inflammatory signalling to NF-kappaB (via IKKbeta-MEKK1) may be down-regulated in early pregnancy, contributing to the immunosuppressive mechanisms which prevail at this time.

L3 ANSWER 4 OF 9 MEDLINE on STN DUPLICATE 4
 ACCESSION NUMBER: 2000115862 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10648602
 TITLE: Activation of the heterodimeric IkappaB kinase alpha (IKKalpha)-IKKbeta complex is directional: IKKalpha regulates IKKbeta under both basal and stimulated conditions.

AUTHOR: O'Mahony A; Lin X; Geleziunas R; Greene W C
 CORPORATE SOURCE: Gladstone Institute of Virology and Immunology, Microbiology and Immunology, University of California, San Francisco, California 94141, USA.

CONTRACT NUMBER: P30A127763
 SOURCE: Molecular and cellular biology, (2000 Feb) Vol. 20, No. 4, pp. 1170-8. Journal code: 8109087. ISSN: 0270-7306.

PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 ENTRY MONTH: 200002
 ENTRY DATE: Entered STN: 29 Feb 2000
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 15 Feb 2000

AB Signal-induced nuclear expression of the eukaryotic NF-kappaB transcription factor involves the stimulatory action of select mitogen-activated protein kinase kinase kinases on the IkappaB kinases (IKKalpha and IKKbeta) which reside in a macromolecular signaling complex termed the signalsome. While genetic studies indicate that IKKbeta is the

principal kinase involved in proinflammatory cytokine-induced IkappaB phosphorylation, the function of the equivalently expressed IKKalpha is less clear. Here we demonstrate that assembly of IKKalpha with IKKbeta in the heterodimeric signalsome serves two important functions: (i) in unstimulated cells, IKKalpha inhibits the constitutive IkappaB kinase activity of IKKbeta; (ii) in activated cells, IKKalpha kinase activity is required for the induction of IKKbeta. The introduction of kinase-inactive IKKalpha, activation loop mutants of IKKalpha, or IKKalpha antisense RNA into 293 or HeLa cells blocks NIK (NF-kappaB-inducing kinase)-induced phosphorylation of the IKKbeta activation loop occurring in functional signalsomes. In contrast, catalytically inactive mutants of IKKbeta do not block NIK-mediated phosphorylation of IKKalpha in these macromolecular signaling complexes. This requirement for kinase-proficient IKKalpha to activate IKKbeta in heterodimeric IKK signalsomes is also observed with other NF-kappaB inducers, including tumor necrosis factor alpha, human T-cell leukemia virus type 1 Tax, Cot, and MEKK1. Conversely, the theta isoform of protein kinase C, which also induces NF-kappaB/Rel, directly targets IKKbeta for phosphorylation and activation, possibly acting through homodimeric IKKbeta complexes. Together, our findings indicate that activation of the heterodimeric IKK complex by a variety of different inducers proceeds in a directional manner and is dependent on the kinase activity of IKKalpha to activate IKKbeta.

L3 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
 ACCESSION NUMBER: 2000:495837 BIOSIS
 DOCUMENT NUMBER: PREV200000495958
 TITLE: The nuclear factor kappa B pathway in human endometrium and first trimester decidua.
 AUTHOR(S): King, A. E. [Reprint author]; Critchley, H. O. D. [Reprint author]; Kelly, R. W. [Reprint author]
 CORPORATE SOURCE: MRC Human Reproductive Sciences Unit and Obstetrics and Gynaecology, Centre for Reproductive Biology, 37 Chalmers Street, Edinburgh, EH3 9ET, UK
 SOURCE: Journal of Reproduction and Fertility Abstract Series, (July, 2000) No. 25, pp. 66-67. print.
 Meeting Info.: Joint Summer Meeting of the Society for the Study of Fertility, the British Andrology Society and the British Fertility Society. Edinburgh, Scotland, UK. July, 2000.
 ISSN: 0954-0725.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 15 Nov 2000
 Last Updated on STN: 10 Jan 2002

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:1086770 CAPLUS
 DOCUMENT NUMBER: 142:173862
 TITLE: Identification and functional characterization of a novel human Misshapen/Nck interacting kinase-related kinase, hMINKp
 AUTHOR(S): Hu, Yuanming; Leo, Cindy; Yu, Simon; Huang, Betty C. B.; Wang, Hank; Shen, Mary; Luo, Ying; Daniel-Issakani, Sarkiz; Payan, Donald G.; Xu, Xiang
 CORPORATE SOURCE: Rigel Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
 SOURCE: Journal of Biological Chemistry (2004), 279(52), 54387-54397
 CODEN: JBCHA3; ISSN: 0021-9258
 PUBLISHER: American Society for Biochemistry and Molecular

DOCUMENT TYPE: Biology
LANGUAGE: Journal
English

AB Misshapen/NIKs-related kinase (MINK) is a member of the germinal center family of kinases that are homologous to the yeast sterile 20 (Ste20) kinases and regulate a wide variety of cellular processes, including cell morphol., cytoskeletal rearrangement, and survival. Here, we present the cloning and functional characterization of a novel human Misshapen/NIKs-related kinase β (hMINK β) that encodes a polypeptide of 1312 amino acids. hMINK β is ubiquitously expressed in most tissues with at least five alternatively spliced isoforms. Similar to Nck interacting kinase (NIK) and Traf2 and Nck-interacting kinase (TNIK), hMINK β moderately activates c-Jun N-terminal kinase (JNK) and assoc. with Nck via the intermediate domain in the yeast two-hybrid system and in a glutathione S-transferase (GST) pull-down assay. Interestingly, overexpression of the kinase domain deleted and kinase-inactive mutants of hMINK β in human fibrosarcoma HT1080 cells enhanced cell spreading, actin stress fiber formation, and adhesion to extracellular matrix, as well as decreased cell motility and cell invasion. Furthermore, these mutants also promoted cell-cell adhesion in human breast carcinoma MCF7 cells, evidenced with cell growth in clusters and increased membrane localization of β -catenin, a multifunctional protein involved in E-cadherin-mediated cell adhesion. Finally, hMINK β protein was found to colocalize with the Golgi apparatus, implicating that hMINK β might exert its functions, at least in part, through the modulation of intracellular protein transport. Taken together, these results suggest that hMINK β plays an important role in cytoskeleton reorganization, cell adhesion, and cell motility.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:561174 CAPLUS

DOCUMENT NUMBER: 135:271044

TITLE: Activation of NF- κ B by nontypeable Hemophilus influenzae is mediated by toll-like receptor 2-TAK1-dependent NIK-IKK α / β -IKB α and MKK3/6-p38 MAP kinase signaling pathways in epithelial cells

AUTHOR(S): Shuto, Tsuyoshi; Xu, Haidong; Wang, Beinan; Han, Jiahui; Kai, Hirofumi; Gu, Xin-Xing; Murphy, Timothy F.; Lim, David J.; Li, Jian-Dong

CORPORATE SOURCE: Gonda Department of Cell and Molecular Biology, House Ear Institute and the Department of Otolaryngology, University of Southern California, Los Angeles, CA, 90057, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2001), 98(15), 8774-8779

CODEN: PNASAG; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nontypeable Hemophilus influenzae (NTHi) is an important human pathogen in both children and adults. In children, it causes otitis media, the most common childhood infection and the leading cause of conductive hearing loss in the United States. In adults, it causes lower respiratory tract infections in the setting of chronic obstructive pulmonary disease, the fourth leading cause of death in the United States. The mol. mechanisms underlying the pathogenesis of NTHi-induced infections remain undefined, but they may involve activation of NF- κ B, a transcriptional activator of multiple host defense genes involved in immune and

inflammatory responses. Here, we show that NTHi strongly activates NF- κ B in human epithelial cells via two distinct signaling pathways, NF- κ B translocation-dependent and -independent pathways. The NF- κ B translocation-dependent pathway involves activation of NF- κ B inducing kinase (NIK)-IKK α /IKK β complex leading to IKK α phosphorylation and degradation, whereas the NF- κ B translocation-independent pathway involves activation of MKK3/6-p38 mitogen-activated protein (MAP) kinase pathway. Bifurcation of NTHi-induced NIK-IKK α /IKK β -IKK α and MKK3/6-p38 MAP kinase pathways may occur at transforming growth factor- β activated kinase 1 (TAK1). Furthermore, we show that toll-like receptor 2 (TLR2) is required for NTHi-induced NF- κ B activation. In addition, several key inflammatory mediators including IL-1 β , IL-8, and tumor necrosis factor- α are up-regulated by NTHi. Finally, P6, a 16-kDa lipoprotein highly conserved in the outer membrane of all NTHi and H. influenzae type b strains, appears to also activate NF- κ B via similar signaling pathways. Taken together, our results demonstrate that NTHi activates NF- κ B via TLR2-TAK1-dependent NIK-IKK α /IKK β -IKK α and MKK3/6-p38 MAP kinase signaling pathways. These studies may bring new insights into mol. pathogenesis of NTHi-induced infections and open up new therapeutic targets for these diseases.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:467814 CAPLUS

DOCUMENT NUMBER: 135:225811

TITLE: Activation of p38, ERK1/2 and NIK Pathways is Required

for IL-1 β and TNF- α -induced Chemokine

Expression in Human Retinal Pigment Epithelial Cells

AUTHOR(S): Bian, Zong-Mei; Elner, Susan G.; Yoshida, Ayako;

Kunkel, Steven L.; Su, Jia; Elner, Victor M.

CORPORATE SOURCE: Department of Ophthalmology, University of Michigan,

Ann Arbor, MI, USA

SOURCE: Experimental Eye Research (2001), 73(1),

111-121

CODEN: EXERA6; ISSN: 0014-4835

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemokine secretion by human retinal pigment epithelium (hRPE) in response to IL-1 β and TNF- α occurs in infectious and noninfectious retinal diseases. In this study, the roles of p38 kinase and extracellular signal-regulated kinase (ERK) signaling pathways were investigated for IL-1 β - or TNF- α -induced IL-8 and MCP-1 secretion by hRPE cells. Treatment of hRPE cells with IL-1 β or TNF- α caused increased steady-state IL-8 and MCP-1 mRNA levels and protein secretion. Stimulation of hRPE with IL-1 β and TNF- α resulted in degradation of IKK α , nuclear translocation of NF- κ B, and prominent increases in p38 and ERK1/2 phosphorylation for as little as 3 min. The induced IL-8 and MCP-1 mRNA and proteins were partially suppressed by U0126, a specific MEK inhibitor, and by SB202190, a selective p38 inhibitor. This induction was completely blocked by simultaneous administration of the two drugs or by incubation with inhibitors for activation of NF- κ B such as BAY11-7085, CAPE, and parthenolide. These results suggest that co-activation of MEK/ERK and p38 pathways as well as activation of NIK pathway are essential for IL-1 β - and TNF- α -stimulation of IL-8 and MCP-1 gene expression in hRPE cells. Furthermore, co-administration of U0126 and SB202190 did not affect the induced degradation of IKK α and NF- κ B nuclear translocation, indicating that NF- κ B is activated by IL-1 β and TNF- α independently of activation of MEK/MAPK and p38

pathways in hRPE cells. (c) 2001 Academic Press.
REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:456596 CAPLUS
DOCUMENT NUMBER: 131:227457
TITLE: Differential I κ B kinase activation and
I κ B α degradation by interleukin-1 β
and tumor necrosis factor- α in human U937
monocytic cells. Evidence for additional regulatory
steps in κ B-dependent transcription
AUTHOR(S): Nasuhara, Yasuyuki; Adcock, Ian M.; Catley, Matthew;
Barnes, Peter J.; Newton, Robert
CORPORATE SOURCE: Department of Thoracic Medicine, National Heart and
Lung Institute, Imperial College School of Medicine,
London, SW3 6LY, UK
SOURCE: Journal of Biological Chemistry (1999),
274(28), 19965-19972
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The I κ B kinases (IKKs) lie downstream of the NF- κ B-inducing
kinase (NIK) and activate NF- κ B by phosphorylation of
I κ B α . This leads to I κ B α degradation and release of
NF- κ B. In U937 monocytic cells, interleukin (IL)-1 β (1 ng/mL)
and tumor necrosis factor (TNF)- α (10 ng/mL) induced
 κ B-dependent transcription equally. However, IKK activity was
strongly induced by TNF- α but not by IL-1 β . This was
consistent with I κ B α phosphorylation and degradation, yet
TNF- α -induced NF- κ B DNA binding was only 30-40% greater than
for IL-1 β . This was not explained by degradation of I κ B β ,
I κ B ϵ , or p105 nor nuclear translocation of
NF- κ B-I κ B α complexes or degradation-independent
release of NF- κ B. Dominant neg. (NIK) repressed TNF- α and
IL-1 β -induced κ B-dependent transcription by .apprx.60% and
.apprx.35%, resp. These data reveal an imprecise relation between IKK
activation, I κ B α degradation, and NF- κ B DNA binding,
suggesting the existence of addnl. mechanisms that regulate NF- κ B
activation. Finally, the lack of correlation between DNA binding and
transcriptional activation plus the fact that Pp1 and genistein both
inhibited κ B-dependent transcription without affecting DNA binding
activity demonstrate the existence of regulatory steps downstream of
NF- κ B DNA binding. Therapeutically these data are important as
inhibition of the NIK-IKK-I κ B α cascade may not produce equivalent
redns. in NF- κ B-dependent gene expression.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> Log Off H
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 17:20:39 ON 24 SEP 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

***** RECONNECTED TO STN INTERNATIONAL *****
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 17:23:32 ON 24 SEP 2008
FILE 'MEDLINE' ENTERED AT 17:23:32 ON 24 SEP 2008
FILE 'BIOSIS' ENTERED AT 17:23:32 ON 24 SEP 2008
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FULL ESTIMATED COST	32.29	32.50
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.20	-3.20

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(FILE 'HOME' ENTERED AT 17:16:24 ON 24 SEP 2008)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 17:16:47 ON 24 SEP 2008

L1 0 S SIRNA (S) NIK AND PD<=20041130
L2 17 S RNA (S) NIK AND PD<=20041130
L3 9 DUP REM L2 (8 DUPLICATES REMOVED)

=> S expression (S) (down-regulat? OR inhibit?) (S) (NIK OR (NF-kappa B inducing kinase)) AND pd<=20041130
1 FILES SEARCHED...
3 FILES SEARCHED...

L4 114 EXPRESSION (S) (DOWN-REGULAT? OR INHIBIT?) (S) (NIK OR (NF-KAPPA B INDUCING KINASE)) AND PD<=20041130

=> Dup Rem L4

PROCESSING COMPLETED FOR L4

L5 45 DUP REM L4 (69 DUPLICATES REMOVED)
ANSWERS '1-24' FROM FILE MEDLINE
ANSWERS '25-32' FROM FILE BIOSIS
ANSWERS '33-42' FROM FILE CAPLUS
ANSWERS '43-45' FROM FILE EMBASE

=> D Ibib abs L5 1-24

L5 ANSWER 1 OF 45 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004312280 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15090542
TITLE: Protein farnesyltransferase inhibitor (SCH 66336) abolishes NF-kappaB activation induced by various carcinogens and inflammatory stimuli leading to suppression of NF-kappaB-regulated gene expression and up-regulation of apoptosis.
AUTHOR: Takada Yasunari; Khuri Fadlo R; Aggarwal Bharat B
CORPORATE SOURCE: Cytokine Research Laboratory, Department of Bioimmunotherapy, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.
CONTRACT NUMBER: P01-CA91844 (United States NCI)

SOURCE: The Journal of biological chemistry, (2004 Jun 18)
Vol. 279, No. 25, pp. 26287-99. Electronic Publication:
2004-04-16.

JOURNAL CODE: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 25 Jun 2004
Last Updated on STN: 25 Jul 2004
Entered Medline: 23 Jul 2004

AB Ras farnesyltransferase inhibitor (FTI) exhibit antiproliferative and antiangiogenic effects through a mechanism that is poorly understood. Because of the known role of Ras in the activation of transcription factor NF-kappaB and because NF-kappaB-regulated genes can control cell survival and angiogenesis, we postulated that FTI mediates its effects in part by modulating NF-kappaB activation. Therefore, in the present study we investigated the effect of FTI, SCH 66336, on NF-kappaB and NF-kappaB-regulated gene expression activated by a variety of inflammatory and carcinogenic agents. We demonstrate by DNA-binding assay that NF-kappaB activation induced by tumor necrosis factor (TNF), phorbol 12-myristate 13-acetate, cigarette smoke, okadaic acid, and H(2)O(2) was completely suppressed by SCH 66336; the suppression was not cell type-specific. This FTI suppressed the activation of IkappaBalpha kinase (IKK), thus abrogating the phosphorylation and degradation of IkappaBalpha. Additionally, TNF-activated Ras and SCH 66336 inhibited the activation. Also, overexpression of Ras (V12) enhanced TNF-induced NF-kappaB activation, and adenoviral dominant-negative Ras (N17) suppressed the activation, thus suggesting the critical role of Ras in TNF signaling. SCH 66336 also inhibited the NF-kappaB-dependent reporter gene expression activated by TNF, TNFR1, TRADD, TRAF2, NIK, and IKK but not that activated by the p65 subunit of NF-kappaB. The TNF-induced NF-kappaB-regulated gene products cyclin D1, COX-2, MMP-9, survivin, IAP1, IAP2, XIAP, Bcl-2, Bfl-1/A1, TRAF1, and FLIP were all down-regulated by SCH 66336, which potentiated apoptosis induced by TNF and doxorubicin. Overall, our results indicate that SCH 66336 inhibited activation of NF-kappaB and NF-kappaB-regulated gene expressions induced by carcinogens and inflammatory stimuli, which may provide a molecular basis for the ability of SCH 66336 to suppress proliferation and angiogenesis.

L5 ANSWER 2 OF 45 MEDLINE ON STN DUPLICATE 2
ACCESSION NUMBER: 2004092153 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14623898
TITLE: Down-regulation of the tumor suppressor PTEN by the tumor necrosis factor-alpha/nuclear factor-kappaB (NF-kappaB)-inducing kinase/NF-kappaB pathway is linked to a default IkappaB-alpha autoregulatory loop.
AUTHOR: Kim Sunghoon; Domon-Dell Claire; Kang Junghee; Chung Dai H; Freund Jean-Noel; Evers B Mark
CORPORATE SOURCE: Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77555-0536, USA.
CONTRACT NUMBER: P30-DK56338 (United States NIDDK)
R01-DK35608 (United States NIDDK)
R01-DK48498 (United States NIDDK)
R37-AG10885 (United States NIA)
SOURCE: The Journal of biological chemistry, (2004 Feb 6)
Vol. 279, No. 6, pp. 4285-91. Electronic Publication:

2003-11-17.
Journal code: 2985121R. ISSN: 0021-9258.
United States
PUB. COUNTRY: Journal; Article; (JOURNAL ARTICLE)
DOCUMENT TYPE: (RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
English
LANGUAGE: Priority Journals
FILE SEGMENT: 200404
ENTRY MONTH: Entered STN: 2 Mar 2004
ENTRY DATE: Last Updated on STN: 2 Apr 2004
Entered Medline: 1 Apr 2004

AB The PTEN (phosphatase and tensin homolog deleted on chromosome ten) tumor suppressor gene affects multiple cellular processes including cell growth, proliferation, and cell migration by antagonizing phosphatidylinositol 3-kinase (PI3K). However, mechanisms by which PTEN expression is regulated have not been studied extensively. Similar to PTEN, tumor necrosis factor-alpha (TNF-alpha) affects a wide spectrum of diseases including inflammatory processes and cancer by acting as a mediator of apoptosis, inflammation, and immunity. In this study, we show that treatment of cancer cell lines with TNF-alpha decreases PTEN expression. In addition, overexpression of TNF-alpha downstream signaling targets, nuclear factor-kappaB (NF-kappaB)-inducing kinase (NIK) and p65 nuclear factor NF-kappaB, lowers PTEN expression, suggesting that TNF-alpha-induced down-regulation of PTEN is mediated through a TNF-alpha/NIK/NF-kappaB pathway. Down-regulation of PTEN by NIK/NF-kappaB results in activation of the PI3K/Akt pathway and augmentation of TNF-alpha-induced PI3K/Akt stimulation. Importantly, we demonstrate that this effect is associated with a lack of an inhibitor of kappaB (IkappaB)-alpha autoregulatory loop. Moreover, these findings suggest the interaction between PI3K/Akt and NF-kappaB via transcriptional regulation of PTEN and offer one possible explanation for increased tumorigenesis in systems in which NF-kappaB is chronically activated. In such a tumor system, these findings suggest a positive feedback loop whereby Akt activation of NF-kappaB further stimulates Akt via down-regulation of the PI3K inhibitor PTEN.

L5 ANSWER 3 OF 45 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004310978 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15212763
TITLE: NF-kappaB inducing kinase activates NF-kappaB transcriptional activity independently of IkappaB kinase gamma through a p38 MAPK-dependent RelA phosphorylation pathway.
AUTHOR: Jijon H; Allard B; Jobin C
CORPORATE SOURCE: Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, University of North Carolina, CB 7032, 7341B Medical Biomolecular Research Building, Chapel Hill, NC 27599-7080, USA.
CONTRACT NUMBER: DK 47700 (United States NIDDK)
SOURCE: Cellular signalling, (2004 Sep) Vol. 16, No. 9, pp. 1023-32.
Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
English
LANGUAGE: Priority Journals
FILE SEGMENT: 200501
ENTRY MONTH: Entered STN: 25 Jun 2004
ENTRY DATE:

Last Updated on STN: 8 Jan 2005

Entered Medline: 7 Jan 2005

AB Molecular and biochemical analysis indicates that nuclear transcription factor kappaB (NF-kappaB)-inducing kinase (NIK) mediates IKK activation and NF-kappaB transcriptional activity. However, gene deletion studies suggest that NIK triggers gene expression without affecting IkappaBalpha degradation and NF-kappaB DNA binding activity. In order to investigate the role of NIK in NF-kappaB transcriptional activity, we used mouse embryonic fibroblasts (MEF) derived from wild-type (wt) and IkappaB kinase gamma (IKKgamma) gene deficient (IKKgamma(-/-)) mice. We report that although TNF-induced NF-kappaB transcriptional activity is abolished in IKKgamma(-/-) cells, adenoviral gene delivery of NIK (Ad5NIK) still enhanced transcriptional activity and IL-6 mRNA accumulation. Moreover, NIK targets the transactivation function of NF-kappaB through stimulation of the transactivation domain (TAD) of RelA (S536) in IKKgamma(-/-) cells. Interestingly, Ad5NIK, but not TNF, induces RelA S536 and p38 mitogen-activated protein kinase (MAPK) phosphorylation in IKKgamma(-/-) cells. Functional analysis demonstrated that Ad5NIK-induced NF-kappaB transcriptional activity, IL-6 mRNA expression and RelA phosphorylation are inhibited by the p38 inhibitor SB203580, suggesting a role for this MAPK in NIK signaling to NF-kappaB. These data demonstrate for the first time the presence of an IKKgamma-independent NIK/p38 MAPK-dependent signaling pathway that activates NF-kappaB and induces pro-inflammatory gene expression through RelA phosphorylation.

L5 ANSWER 4 OF 45 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004309723 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14742314
TITLE: An acyclic retinoid, NIK-333, inhibits N-diethylnitrosamine-induced rat hepatocarcinogenesis through suppression of TGF-alpha expression and cell proliferation.
AUTHOR: Kagawa Masataka; Sano Tetsuro; Ishibashi Naoto; Hashimoto Manabu; Okuno Masataka; Moriaki Hisataka; Suzuki Rikako; Kohno Hiroyuki; Tanaka Takuji
CORPORATE SOURCE: Pharmaceutical Research Laboratories, Nikken Chemicals Co. Ltd, 1-346 Kitabukuro-cho, Omiya-ku, Saitama-shi, Saitama 330-0835, Japan.
SOURCE: Carcinogenesis, (2004 Jun) Vol. 25, No. 6, pp. 979-85. Electronic Publication: 2004-01-23. Journal code: 8008055. ISSN: 0143-3334.
PUB. COUNTRY: England; United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 25 Jun 2004
Last Updated on STN: 16 Jul 2004
Entered Medline: 15 Jul 2004

AB The present study was designed to determine the effects of NIK-333, a synthetic acyclic retinoid, on N-diethylnitrosamine (DEN)-induced hepatocarcinogenesis in male F344 rats. Animals were given DEN dissolved in drinking water at a concentration of 40 p.p.m. for 5 weeks and then provided with drinking water free of DEN for 15 weeks to induce hepatocellular neoplasms. NIK-333 was administered orally (once a day) to rats at doses of 10, 40 and 80 mg/kg body wt for 14 weeks, starting 1 week after the completion of administration of DEN. At 20 weeks after the start of DEN administration, histopathological evaluation was carried out on all animals. The effects of NIK-333 on the cell proliferation activity of non-tumorous areas and liver tumor cells and the immunohistochemical

expression of transforming growth factor-alpha (TGF-alpha) were also evaluated. NIK-333 at 40 and 80 mg/kg body wt significantly inhibited hepatocarcinogenesis ($P < 0.05$). In addition, NIK-333 at the same doses decreased DEN-induced overexpression of TGF-alpha in hepatocellular neoplasms (adenomas and carcinomas) and their surrounding tissue. Furthermore, NIK-333 significantly inhibited cell proliferation activity in the lesions and in non-tumorous areas ($P < 0.01$). Our results suggest that NIK-333 inhibits DEN-induced hepatocarcinogenesis through suppression of TGF-alpha expression and cell proliferation.

L5 ANSWER 5 OF 45 MEDLINE on STN DUPLICATE 7
 ACCESSION NUMBER: 2004449137 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15356994
 TITLE: Suppression of protein kinase C and nuclear oncogene expression as possible action mechanisms of cancer chemoprevention by Curcumin.
 AUTHOR: Lin Jen-Kun
 CORPORATE SOURCE: Institutes of Biochemistry, College of Medicine, National Taiwan University, No.1, Section 1, Jen-ai Road, Taipei, Taiwan, 10018.. jklin@ha.mc.ntu.edu.tw
 SOURCE: Archives of pharmacol research, (2004 Jul) Vol. 27, No. 7, pp. 683-92. Ref: 63
 Journal code: 8000036. ISSN: 0253-6269.
 PUB. COUNTRY: Korea (South)
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200502
 ENTRY DATE: Entered STN: 11 Sep 2004
 Last Updated on STN: 19 Feb 2005
 Entered Medline: 18 Feb 2005
 AB Curcumin (diferuloylmethane) is a major naturally-occurring polyphenol of Curcuma species, which is commonly used as a yellow coloring and flavoring agent in foods. Curcumin has shown anti-carcinogenic activity in animal models. Curcumin possesses anti-inflammatory activity and is a potent inhibitor of reactive oxygen-generating enzymes such as lipoygenase/cyclooxygenase, xanthine dehydrogenase/oxidase and inducible nitric oxide synthase; and an effective inducer of heme oxygenase-1. Curcumin is also a potent inhibitor of protein kinase C (PKC), EGF(Epidermal growth factor)-receptor tyrosine kinase and IkappaB kinase. Subsequently, curcumin inhibits the activation of NF(nuclear factor)kappaB and the expressions of oncogenes including c-jun, c-fos, c-myc, NIK, MAPKs, ERK, ELK, PI3K, Akt, CDKs and iNOS. It is proposed that curcumin may suppress tumor promotion through blocking signal transduction pathways in the target cells. The oxidant tumor promoter TPA activates PKC by reacting with zinc thiolates present within the regulatory domain, while the oxidized form of cancer chemopreventive agent such as curcumin can inactivate PKC by oxidizing the vicinal thiols present within the catalytic domain. Recent studies indicated that proteasome-mediated degradation of cell proteins play a pivotal role in the regulation of several basic cellular processes including differentiation, proliferation, cell cycling, and apoptosis. It has been demonstrated that curcumin-induced apoptosis is mediated through the impairment of ubiquitin-proteasome pathway. Curcumin was first biotransformed to dihydrocurcumin and tetrahydrocurcumin and that these compounds subsequently were converted to monoglucuronide conjugates. These results suggest that curcumin-glucuronide, dihydrocurcumin-glucuronide, tetrahydrocurcumin-glucuronide and tetrahydrocurcumin are the major metabolites of curcumin in mice, rats and humans.

L5 ANSWER 6 OF 45 MEDLINE on STN DUPLICATE 8
 ACCESSION NUMBER: 2004556833 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15528996
 TITLE: IKKgamma inhibits activation of NF-kappaB by NIK.
 AUTHOR: Kwon Woo Jong; Kim Sun Hee; Park Yeo Ok; Cho Mong; Kang Chi Dug; Lee Gwang; An Woo Gun; Joo Woo Hong; Kim Dong Wan
 CORPORATE SOURCE: Department of Microbiology, College of Natural Sciences, Changwon National University, Changwon 641-773, Korea.
 SOURCE: Molecules and cells, (2004 Oct 31) Vol. 18, No. 2, pp. 200-6.
 Journal code: 9610936. ISSN: 1016-8478.
 PUB. COUNTRY: Korea (South)
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200504
 ENTRY DATE: Entered STN: 6 Nov 2004
 Last Updated on STN: 6 Apr 2005
 Entered Medline: 5 Apr 2005
 AB IKKgamma is a component of the IKK complex, which regulates NF-kappaB activity. To investigate the role of IKKgamma, we expressed wild type IKKgamma containing 412 amino acids, and deletion mutants containing residues 1-312 and 101-412, using murine IKKgamma cDNA. In a co-transfection assay with a CAT reporter plasmid, NIK activated NF-kappaB-dependent gene expression approximately two fold and this expression was inhibited by co-transfection of a wild type IKKgamma expression plasmid. In binding assays IKKgamma inhibited the association of IkappaBalpha with IKKbeta and the subsequent phosphorylation of IkappaBalpha that is activated by NIK. Inhibition by IKKgamma also occurred in an assay with a dominant negative mutant of NIK but not with a C-terminal deletion mutant of IKKgamma, indicating that the C-terminal 100 amino acids of IKKgamma are important for negative regulation of NF-kappaB activation. In addition, the interaction of IKKbeta with IKKgamma was inhibited by co-transfection with a NIK expression plasmid. Our results suggest that overexpression of IKKgamma inhibits activation of NF-kappaB by NIK by competing with NIK for interaction with IKKbeta.

L5 ANSWER 7 OF 45 MEDLINE on STN DUPLICATE 10
 ACCESSION NUMBER: 2003313883 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12729461
 TITLE: Fractalkine (CX3CL1) stimulated by nuclear factor kappaB (NF-kappaB)-dependent inflammatory signals induces aortic smooth muscle cell proliferation through an autocrine pathway.
 AUTHOR: Chandrasekar Bysani; Mummidi Srinivas; Perla Rao P; Bysani Sailaja; Dulin Nikolai O; Liu Feng; Melby Peter C
 CORPORATE SOURCE: Department of Medicine, University of Texas Health Science Center, San Antonio, TX 78229, USA..
 chandraseka@uthscsa.edu
 CONTRACT NUMBER: HL68020 (United States NHLBI)
 SOURCE: The Biochemical journal, (2003 Jul 15) Vol. 373, No. Pt 2, pp. 547-58.
 Journal code: 2984726R. ISSN: 0264-6021.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals

ENTRY MONTH: 200308

ENTRY DATE: Entered STN: 8 Jul 2003

Last Updated on STN: 16 Aug 2003

Entered Medline: 15 Aug 2003

AB Fractalkine (also known as CX3CL1), a CX3C chemokine, activates and attracts monocytes/macrophages to the site of injury/inflammation. It binds to CX3C receptor 1 (CX3CR1), a pertussis toxin-sensitive G-protein-coupled receptor. In smooth muscle cells (SMCs), fractalkine is induced by proinflammatory cytokines [tumour necrosis factor-alpha (TNF-alpha) and interferon-gamma (IFN-gamma)], which may mediate monocyte adhesion to SMCs. However, the mechanisms underlying its induction are unknown. In addition, it is unclear whether SMCs express CX3CR1. TNF-alpha activated nuclear factor kappaB (NF-kappaB) and induced fractalkine and CX3CR1 expression in a time-dependent manner in rat aortic SMCs. Transient transfections with dominant-negative (dn) inhibitory kappaB (IkappaB)-alpha, dnIkappaB-beta, dnIkappaB kinase (IKK)-gamma, kinase-dead (kd) NF-kappaB-inducing kinase (NIK) and kdIKK-beta, or pretreatment with wortmannin, Akt inhibitor, pyrrolidinecarbodithioc acid ammonium salt ('PDTTC') or MG-132, significantly attenuated TNF-alpha-induced fractalkine and CX3CR1 expression. Furthermore, expression of dn TNF-alpha-receptor-associated factor 2 (TRAF2), but not dnTRAF6, inhibited TNF-alpha signal transduction. Pretreatment with pertussis toxin or neutralizing anti-CX3CR1 antibodies attenuated TNF-alpha-induced fractalkine expression, indicating that fractalkine autoregulation plays a role in TNF-alpha-induced sustained fractalkine expression. Fractalkine induced its own expression, via pertussis toxin-sensitive G-proteins, phosphoinositide 3-kinase (PI 3-kinase), phosphoinositide-dependent kinase 1 (PDK1), Akt, NIK, IKK and NF-kappaB activation, and induced SMC cell-cell adhesion and cellular proliferation. Taken together, our results demonstrate that TNF-alpha induces the expression of fractalkine and CX3CR1 in rat aortic SMCs and that this induction is mediated by NF-kappaB activation. We also show that fractalkine induces its own expression, which is mediated by the PI 3-kinase/PDK1/Akt/NIK/IKK/NF-kappaB signalling pathway. More importantly, fractalkine increased cell-cell adhesion and aortic SMC proliferation, indicating a role in initiation and progression of atherosclerotic vascular disease.

L5 ANSWER 8 OF 45

MEDLINE on STN

DUPLICATE 11

ACCESSION NUMBER: 2003125422 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12639713

TITLE: Induction of cyclooxygenase-2 by lipopolysaccharide in canine tracheal smooth muscle cells: involvement of p42/p44 and p38 mitogen-activated protein kinases and nuclear factor-kappaB pathways.

AUTHOR: Luo Shue-Fen; Wang Chuan-Chwan; Chien Chin-Sung; Hsiao Li-Der; Yang Chuen-Mao

CORPORATE SOURCE: Department of Internal Medicine, College of Medicine, Chang Gung University, Kwei-San, Tao-Yuan, Taiwan.

SOURCE: Cellular signalling, (2003 May) Vol. 15, No. 5, pp. 497-509.

Journal code: 8904683. ISSN: 0898-6568.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200310

ENTRY DATE: Entered STN: 18 Mar 2003

Last Updated on STN: 15 Oct 2003

Entered Medline: 14 Oct 2003

AB Lipopolysaccharide (LPS) was found to induce inflammatory responses in the

airways and exerted as a potent stimulus for PG synthesis. This study was to determine the mechanisms of LPS-enhanced cyclooxygenase (COX)-2 expression associated with PGE(2) synthesis in tracheal smooth muscle cells (TSMCs). LPS markedly increased the expression of COX-2 and release of PGE(2) in a time- and concentration-dependent manner, whereas COX-1 remained unaltered. Both the expression of COX-2 and the generation of PGE(2) in response to LPS were attenuated by a tyrosine kinase inhibitor genistein, a phosphatidylcholine-phospholipase C inhibitor D609, a phosphatidylinositol-phospholipase C inhibitor U73122, protein kinase C inhibitors, GF109203X and staurosporine, removal of Ca(2+) by addition of BAPTA/AM plus EGTA, and phosphatidylinositol 3-kinase (PI3-K) inhibitors, LY294002 and wortmannin. Furthermore, LPS-induced NF-kappaB activation correlated with the degradation of IkappaB-alpha, COX-2 expression, and PGE(2) synthesis, was inhibited by transfection with dominant negative mutants of NIK and IKK-alpha, but not by IKK-beta. LPS-induced COX-2 expression and PGE(2) synthesis were completely inhibited by PD98059 (an inhibitor of MEK1/2) and SB203580 (an inhibitor of p38 MAPK inhibitor), but these two inhibitors had no effect on LPS-induced NF-kappaB activation, indicating that NF-kappaB is activated by LPS independently of activation of p42/p44 MAPK and p38 MAPK pathways in TSMCs. Taken together, these findings suggest that the increased expression of COX-2 correlates with the release of PGE(2) from LPS-challenged TSMCs, at least in part, independently mediated through MAPKs and NF-kappaB signalling pathways. LPS-mediated responses were modulated by PLC, Ca(2+), PKC, tyrosine kinase, and PI3-K in these cells.

L5	ANSWER 9 OF 45	MEDLINE on STN	DUPLICATE 12
ACCESSION NUMBER:	2003354061	MEDLINE	
DOCUMENT NUMBER:	PubMed ID: 12716652		
TITLE:	Stretch-induced IL-8 depends on c-Jun NH2-terminal and nuclear factor-kappaB-inducing kinases.		
AUTHOR:	Li Li-Fu; Ouyang Bin; Choukroun Gabriel; Matyal Robina; Mascarenhas Marcella; Jafari Behrouz; Bonventre Joseph V; Force Thomas; Quinn Deborah A		
CORPORATE SOURCE:	Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.		
CONTRACT NUMBER:	HL-039020 (United States NHLBI) HL-61688 (United States NHLBI) HL-67371 (United States NHLBI)		
SOURCE:	American journal of physiology. Lung cellular and molecular physiology, (2003 Aug) Vol. 285, No. 2, pp. L464-75. Electronic Publication: 2003-04-25. Journal code: 100901229. ISSN: 1040-0605.		
PUB. COUNTRY:	United States		
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)		
LANGUAGE:	English		
FILE SEGMENT:	Priority Journals		
ENTRY MONTH:	200309		
ENTRY DATE:	Entered STN: 31 Jul 2003 Last Updated on STN: 1 Oct 2003 Entered Medline: 30 Sep 2003		
AB	Positive pressure ventilation with large tidal volumes has been shown to cause release of cytokines, including interleukin (IL)-8. The mechanisms regulating lung stretch-induced cytokine production are unclear. We hypothesized that stretch-induced IL-8 production is dependent on the activation of the mitogen-activated protein kinases, c-Jun NH2-terminal kinases (JNK), p38, and/or extracellular signal-regulated kinase (ERK) 1/2. We exposed A549 cells, a type II-like alveolar epithelial cell line, to cyclic stretch at 20 cycles/min for 5 min-2 h. Cyclic stretch induced IL-8 protein production, IL-8 mRNA expression, and JNK activation, but		

only transient activation of p38 and ERK1/2. Inhibition of stretch-induced JNK activation by adenovirus-mediated gene transfer of stress-activated protein kinase (SEK-1), a dominant-negative mutant of SEK-1, the immediate upstream activator of the JNKs, and pharmacological JNK inhibitor II SP-600125 blocked IL-8 mRNA expression and attenuated IL-8 production. Inhibition of p38 and ERK1/2 did not affect stretch-induced IL-8 production. Stretch-induced activation NF-kappaB and activator protein (AP)-1 was blocked by NF-kappaB inhibitor and JNK inhibitor, respectively. An NF-IL-6 site was not essential for cyclic stretch-induced IL-8 promoter activity. Stretch also induced NF-kappaB-inducing kinase (NIK) activation, and inhibition of NF-kappaB attenuated IL-8 mRNA expression and IL-8 production. We conclude that stretch-induced transcriptional regulation of IL-8 mRNA and IL-8 production was via activation of AP-1 and NF-kappaB and was dependent on JNK and NIK activation, respectively.

L5 ANSWER 10 OF 45 MEDLINE on STN DUPLICATE 14
 ACCESSION NUMBER: 2002342279 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12085227
 TITLE: Constitutive activation of NF-kappaB in Ki-ras-transformed prostate epithelial cells.
 AUTHOR: Kim Bo-Yeon; Gaynor Richard B; Song Kyung; Dritschilo Anatoly; Jung Mira
 CORPORATE SOURCE: Department of Radiation Medicine, Georgetown University School of Medicine, Washington DC 20007, USA.
 CONTRACT NUMBER: CA45408 (United States NCI)
 CA74175 (United States NCI)
 SOURCE: Oncogene, (2002 Jul 4) Vol. 21, No. 29, pp. 4490-7.
 Journal code: 8711562. ISSN: 0950-9232.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200207
 ENTRY DATE: Entered STN: 27 Jun 2002
 Last Updated on STN: 19 Sep 2002
 Entered Medline: 19 Jul 2002

AB The signaling pathway responsible for the activation of nuclear factor-kappaB (NF-kappaB) by oncogenic forms of Ras remains unclear. Both, the transactivation and DNA binding activities of NF-kappaB, were increased in 267B1 human prostate epithelial cells transformed by viral Kirsten-ras (267B1/Ki-ras cells) compared with those in the parental cells. This increased NF-kappaB activity was attributed to a heterodimeric complex of p50 and p65 subunits. Although the abundance of the inhibitor protein IkappaBbeta was higher in 267B1/Ki-ras cells than in 267B1 cells, an electrophoretic mobility-shift assay suggested that IkappaBalpha is responsible for the activation of NF-kappaB in the former cells. Consistent with this notion, the phosphorylation of IkappaBalpha appeared increased in 267B1/Ki-ras cells, and the proteasome inhibitor I abolished the constitutive activation of NF-kappaB in these cells. The expression of dominant negative mutants of either NIK (NF-kappaB-inducing kinase) or IKKbeta (IkappaB kinase beta) inhibited the activity of NF-kappaB in 267B1/Ki-ras cells. Furthermore, chemical inhibitors specific for Ras activation, sulindac sulfide and farnesyltransferase inhibitor I, markedly reduced IkappaBalpha phosphorylation and NF-kappaB activation in the Ki-ras-transformed cells while transfection of these cells with NIK or IKKbeta counteracted the inhibitory effect on NF-kappaB activation. These results suggest that oncogenic Ki-Ras induces transactivation of NF-kappaB through the NIK-IKKbeta-IkappaBalpha pathway.

L5 ANSWER 11 OF 45 MEDLINE on STN DUPLICATE 15
 ACCESSION NUMBER: 2002461760 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12220616
 TITLE: Interleukin-1beta-induced cyclooxygenase-2 expression is mediated through activation of p42/44 and p38 MAPKs, and NF-kappaB pathways in canine tracheal smooth muscle cells.
 AUTHOR: Yang Chuen-Mao; Chien Chin-Sung; Hsiao Li-Der; Luo Shu-Fen; Wang Chuan-Chwan
 CORPORATE SOURCE: Department of Physiology and Pharmacology, College of Medicine, Chang Gung University, Kwei-San, Tao-Yuan, Taiwan.. chuenmao@mail.cgu.edu.tw
 SOURCE: Cellular signalling, (2002 Nov) Vol. 14, No. 11, pp. 899-911.
 Journal code: 8904683. ISSN: 0898-6568.
 PUB. COUNTRY: England; United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200304
 ENTRY DATE: Entered STN: 11 Sep 2002
 Last Updated on STN: 19 Apr 2003
 Entered Medline: 18 Apr 2003

AB Interleukin-beta (IL-1beta) was found to induce inflammatory responses in the airways, which exerted a potent stimulus for PG synthesis. This study was to determine the mechanisms of IL-1beta-enhanced cyclooxygenase (COX)-2 expression associated with PGE(2) synthesis in tracheal smooth muscle cells (TSMCs). IL-1beta markedly increased COX-2 expression and PGE(2) formation in a time- and concentration-dependent manner in TSMCs. Both COX-2 expression and PGE(2) formation in response to IL-1beta were attenuated by a tyrosine kinase inhibitor, genistein, a phosphatidylcholine-phospholipase C inhibitor, D609, a phosphatidylinositol-phospholipase C inhibitor, U73122, protein kinase C inhibitors, GF109203X and staurosporine, removal of Ca(2+) by addition of BAPTA/AM plus EGTA, and phosphatidylinositol 3-kinase (PI3-K) inhibitors, LY294002 and wortmannin. IL-1beta-induced activation of NF-kappaB correlated with the degradation of I-kappaB-alpha in TSMCs. IL-1beta-induced NF-kappaB activation, COX-2 expression, and PGE(2) synthesis were inhibited by the dominant negative mutants of NIK and IKK-alpha, but not by IKK-beta. IL-1beta-induced COX-2 expression and PGE(2) synthesis were completely inhibited by PD98059 (an inhibitor of MEK1/2) and SB203580 (an inhibitor of p38 inhibitor), but these two inhibitors had no effect on IL-1beta-induced NF-kappaB activation, indicating that activation of p42/44 and p38 MAPK and NF-kappaB signalling pathways were independently required for these responses. These findings suggest that the increased expression of COX-2 correlates with the release of PGE(2) from IL-1beta-challenged TSMCs, at least in part, independently mediated through MAPKs and NF-kappaB signalling pathways in canine TSMCs. IL-1beta-mediated responses were modulated by PLC, Ca(2+), PKC, tyrosine kinase, and PI3-K in these cells.

L5 ANSWER 12 OF 45 MEDLINE on STN DUPLICATE 16
 ACCESSION NUMBER: 2002312589 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12055104
 TITLE: Differential requirement for NF-kappaB-inducing kinase in the induction of NF-kappaB by IL-1beta, TNF-alpha, and Fas.
 AUTHOR: Russo Maria P; Bennett Brydon L; Manning Anthony M; Brenner David A; Jobin Christian
 CORPORATE SOURCE: Department of Medicine and Center for Gastrointestinal Biology and Disease, University of North Carolina, Chapel Hill, North Carolina 27599-7080, USA.

CONTRACT NUMBER: R01-DK47700 (United States NIDDK)
 SOURCE: American journal of physiology. Cell physiology, (2002 Jul) Vol. 283, No. 1, pp. C347-57.
 Journal code: 100901225. ISSN: 0363-6143.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200207
 ENTRY DATE: Entered STN: 11 Jun 2002
 Last Updated on STN: 17 Jul 2002
 Entered Medline: 16 Jul 2002

AB In this study, we examined the role of the nuclear factor-kappaB (NF-kappaB)-inducing kinase (NIK) in distinct signaling pathways leading to NF-kappaB activation. We show that a dominant-negative form of NIK (dnNIK) delivered by adenoviral (Ad5dnNIK) vector inhibits Fas-induced IkappaBalpha phosphorylation and NF-kappaB-dependent gene expression in HT-29 and HeLa cells. Interleukin (IL)-1beta- and tumor necrosis factor-alpha (TNF-alpha)-induced NF-kappaB activation and kappaB-dependent gene expression are inhibited in HeLa cells but not in Ad5dnNIK-infected HT-29 cells. Moreover, Ad5dnNIK failed to sensitize HT-29 cells to TNF-alpha-induced apoptosis at an early time point. However, cytokine- and Fas-induced signals to NF-kappaB are finally integrated by the IkappaB kinase (IKK) complex, since IkappaBalpha phosphorylation, NF-kappaB DNA binding activity, and IL-8 gene expression were strongly inhibited in HT-29 and HeLa cells overexpressing dominant-negative IKKbeta (Ad5dnIKKbeta). Our findings support the concept that cytokine signaling to NF-kappaB is redundant at the level of NIK. In addition, this study demonstrates for the first time the critical role of NIK and IKKbeta in Fas-induced NF-kappaB signaling cascade.

L5 ANSWER 13 OF 45 MEDLINE on STN DUPLICATE 18
 ACCESSION NUMBER: 2001291007 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11278990
 TITLE: Inhibition of the nuclear factor kappa B (NF-kappa B) pathway by tetracyclic kaurene diterpenes in macrophages. Specific effects on NF-kappa B-inducing kinase activity and on the coordinate activation of ERK and p38 MAPK.
 AUTHOR: Castriello A; de Las Heras B; Hortelano S; Rodriguez B; Villar A; Bosca L
 CORPORATE SOURCE: Instituto de Bioquímica, Centro Mixto Consejo Superior de Investigaciones Científicas-Universidad Complutense de Madrid, Spain.
 SOURCE: The Journal of biological chemistry, (2001 May 11) Vol. 276, No. 19, pp. 15854-60. Electronic Publication: 2001-02-09.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200106
 ENTRY DATE: Entered STN: 18 Jun 2001
 Last Updated on STN: 5 Jan 2003
 Entered Medline: 14 Jun 2001

AB The anti-inflammatory action of most terpenes has been explained in terms of the inhibition of nuclear factor kappaB (NF-kappaB) activity. Ent-kaurene diterpenes are intermediates of the synthesis of giberellins and inhibit the expression of NO synthase-2 and the release of tumor

necrosis factor- α in J774 macrophages challenged with lipopolysaccharide. These diterpenes inhibit NF- κ B and IkappaB kinase (IKK) activation in vivo but failed to affect in vitro the function of NF- κ B, the phosphorylation and targeting of IkappaB α , and the activity of IKK-2. Transient expression of NF- κ B-inducing kinase (NIK) activated the IKK complex and NF- κ B, a process that was inhibited by kaurenes, indicating that the inhibition of NIK was one of the targets of these diterpenes. These results show that kaurenes impair the inflammatory signaling by inhibiting NIK, a member of the MAPK kinase superfamily that interacts with tumor necrosis factor receptor-associated factors, and mediate the activation of NF- κ B by these receptors. Moreover, kaurenes delayed the phosphorylation of p38, ERK1, and ERK2 MAPKs, but not that of JNK, in response to lipopolysaccharide treatment of J774 cells. The absence of a coordinate activation of MAPK and IKK might contribute to a deficient activation of NF- κ B that is involved in the anti-inflammatory activity of these molecules.

L5 ANSWER 14 OF 45 MEDLINE on STN DUPLICATE 19
 ACCESSION NUMBER: 2001208143 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11254583
 TITLE: Micrococci and peptidoglycan activate TLR2-->MyD88-->IRAK-->TRAF-->NIK-->IKK-->NF- κ B signal transduction pathway that induces transcription of interleukin-8.
 AUTHOR: Wang Q; Dziarski R; Kirschning C J; Muzio M; Gupta D
 CORPORATE SOURCE: Northwest Center for Medical Education, Indiana University School of Medicine, Gary, Indiana 46408, USA.
 CONTRACT NUMBER: AI28797 (United States NIAID)
 SOURCE: Infection and immunity, (2001 Apr) Vol. 69, No. 4, pp. 2270-6.
 Journal code: 0246127. ISSN: 0019-9567.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200104
 ENTRY DATE: Entered STN: 17 Apr 2001
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 12 Apr 2001

AB This study was done to elucidate the signal transduction pathway of interleukin-8 (IL-8) induction by gram-positive bacteria. Bacteria (micrococci) and peptidoglycan (PGN) induced transcription of IL-8 in HEK293 cells expressing Toll-like receptor 2 (TLR2) and CD14 but not in those expressing TLR1 or TLR4. A mutation within the NF- κ B site in the IL-8 promoter abrogated transcriptional induction of IL-8 by the two stimulants. Dominant negative myeloid differentiation protein (MyD88), IL-1 receptor-associated kinase (IRAK), NF- κ B-inducing kinase (NIK), and IkappaB kinase (IKK) mutant forms completely inhibited micrococci- and PGN-induced activation of NF- κ B and expression of the gene for IL-8. Induction of NF- κ B was partially inhibited by dominant negative tumor necrosis factor receptor-associated kinase 6 (TRAF6) but not TRAF2, whereas induction of IL-8 gene was partially inhibited by both TRAF6 and TRAF2. These data indicate that micrococci and PGN induce TLR2-dependent activation of the gene for IL-8 and that this activation requires MyD88, IRAK, NIK, IKK, and NF- κ B and may also utilize TRAF6 and, to a lesser extent, TRAF2.

L5 ANSWER 15 OF 45 MEDLINE on STN DUPLICATE 20
 ACCESSION NUMBER: 2001466101 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11510478
 TITLE: Modulation of gene expression by (-)-epigallocatechin

gallate in PC-9 cells using a cDNA expression array.
 AUTHOR: Okabe S; Fujimoto N; Sueoka N; Suganuma M; Fujiki H
 CORPORATE SOURCE: Saitama Cancer Center, Japan.
 SOURCE: Biological & pharmaceutical bulletin, (2001 Aug)
 Vol. 24, No. 8, pp. 883-6.
 Journal code: 9311984. ISSN: 0918-6158.
 Japan
 PUB. COUNTRY:
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200201
 ENTRY DATE: Entered STN: 21 Aug 2001
 Last Updated on STN: 28 Jan 2002
 Entered Medline: 23 Jan 2002

AB Green tea is the most effective cancer preventive beverage. In the light of this, the mechanisms of action of tea polyphenols were investigated on the molecular levels. We present here the effects of (-)-epigallocatechin gallate (EGCG) on expression of 588 genes in human lung cancer cell line PC-9 cells, using a human cancer cDNA expression array. The levels of gene expression in non-treated control cells, and cells treated with EGCG alone, with the tumor promoter okadaic acid alone, and with EGCG plus okadaic acid, were studied, and their expression levels were classified into down-regulation (under 0.5 fold) and up-regulation (over 2.0 fold) by comparing with the levels of control. Non-treated PC-9 cells expressed 163 genes out of 588, and EGCG-treated cells induced down-regulated expression of 12 genes and up-regulated expression of 4 other genes. From a comparison of gene expression in the cells treated with EGCG and in cells treated with EGCG plus okadaic acid, we found the following genes commonly affected by EGCG: down-regulation of four genes, NF-kappaB inducing kinase (NIK), death-associated protein kinase 1 (DAPK 1), rhoB and tyrosine-protein kinase (SKY); up-regulation of one gene, retinoic acid receptor alpha. Among them, we think down-regulation of NIK gene expression is significant for cancer prevention, based on evidence that inhibition of NF-kappaB activation is a result of inhibition of NIK/IKK signalling complex.

L5 ANSWER 16 OF 45 MEDLINE on STN DUPLICATE 21
 ACCESSION NUMBER: 2003402255 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 12940066
 TITLE: Effect of mm-LDL on NF-kB activation in endothelial cell.
 AUTHOR: Yin H C; Liu X Y; Liu P M; Zhang H; Liang P; Wang Z L; She M P
 CORPORATE SOURCE: Department of Pathology, Institute of Basic Medical Sciences, CAMS and PUMC, Beijing 100005, China.
 SOURCE: Zhongguo yi xue ke xue yuan xue bao. Acta Academiae Mediciniae Sinicae, (2001 Aug) Vol. 23, No. 4, pp. 312-6.
 Journal code: 8006230. ISSN: 1000-503X.
 PUB. COUNTRY: China
 DOCUMENT TYPE: (COMPARATIVE STUDY)
 (ENGLISH ABSTRACT)
 Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: Chinese
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200406
 ENTRY DATE: Entered STN: 28 Aug 2003
 Last Updated on STN: 11 Jun 2004
 Entered Medline: 10 Jun 2004

AB OBJECTIVE: To investigate the signal transduction pathway of NF-kB

activated by minimally modified low density lipoprotein (mm-LDL) in endothelial cells and the effect of NF-kB on platelet derived growth factor b (PDGFB) mRNA expression. METHODS: mm-LDL was prepared through iron oxidation by dialyzing the native LDL against FeSO4 in PBS. Endothelial cells were incubated in a medium containing mm-LDL, TNF, and IL-1 respectively and electrophoretic mobility shift assay (EMSA) was displayed to check on the activation of NF-kB. Luciferase reporter gene was analysed to investigate the effect of nuclear factor inducing kinase (NIK), inhibitor of NF-kB kinase alpha (IKK alpha) and inhibitor of NF-kB kinase beta (IKK beta) on NF-kB activation. In addition, endothelial cells were transfected using PDGFB promoter-luciferase for reporter gene analysis or transfected with mut-NIK for slot blot analysis to study the effect of NF-kB on PDGFB mRNA expression. RESULTS: mm-LDL was able to activate NF-kB in endothelial cells. mut-NIK and mut-IKK beta inhibited luciferase activity induced by mm-LDL. mm-LDL could also enhance luciferase activity controlled by upstream sequence of PDGFB promoter which contains element interacting with NF-kB. Result of slot blot showed inhibition of PDGFB mRNA expression by mut-NIK in the endothelial cells stimulated by mm-LDL. CONCLUSION: mm-LDL may activate NF-kB through NIK-IKK beta pathway and promote PDGFB mRNA expression in endothelial cells.

L5 ANSWER 17 OF 45 MEDLINE on STN DUPLICATE 22
 ACCESSION NUMBER: 2001112017 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11136824
 TITLE: Modulation of the nuclear factor kappa B pathway by Shp-2 tyrosine phosphatase in mediating the induction of interleukin (IL)-6 by IL-1 or tumor necrosis factor.
 AUTHOR: You M; Flick L M; Yu D; Feng G S
 CORPORATE SOURCE: Burnham Institute, La Jolla, California 92037, USA.
 CONTRACT NUMBER: CA78606 (United States NCI)
 SOURCE: GM53660 (United States NIGMS)
 The Journal of experimental medicine, (2001 Jan 1)
 Vol. 193, No. 1, pp. 101-10.
 Journal code: 2985109R. ISSN: 0022-1007.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200102
 ENTRY DATE: Entered STN: 22 Mar 2001
 Last Updated on STN: 22 Mar 2001
 Entered Medline: 8 Feb 2001
 AB Shp-2, a src homology (SH)2-containing phosphotyrosine phosphatase, appears to be involved in cytoplasmic signaling downstream of a variety of cell surface receptors, although the mechanism is unclear. Here, we have determined a role of Shp-2 in the cytokine circuit for inflammatory and immune responses. Production of interleukin (IL)-6 in response to IL-1 alpha or tumor necrosis factor (TNF)-alpha was nearly abolished in homozygous mutant (Shp-2(-/-)) fibroblast cells. The targeted Shp-2 mutation has no significant effect on the activation of the three types of mitogen-activated protein (MAP) kinases, extracellular signal-regulated kinase (Erk), c-Jun NH(2)-terminal kinase (Jnk), and p38, by IL-1/TNF, indicating that Shp-2 does not work through MAP kinase pathways in mediating IL-1/TNF-induced IL-6 synthesis. In contrast, IL-1/TNF-stimulated nuclear factor (NF)-kappa B DNA binding activity and inhibitor of kappa B (I kappa B) phosphorylation was dramatically decreased in Shp-2(-/-) cells, while the expression and activity of NF-kappa B-inducing kinase (NIK), Akt, and I kappa B kinase (IKK) were not changed. Reintroduction of a wild-type Shp-2 protein into Shp-2(-/-)

cells rescued NF-kappa B activation and IL-6 production in response to IL-1/TNF stimulation. Furthermore, Shp-2 tyrosine phosphatase was detected in complexes with IKK as well as with IL-1 receptor. Thus, this SH2-containing enzyme is an important cytoplasmic factor required for efficient NF-kappa B activation. These results elucidate a novel mechanism of Shp-2 in cytokine signaling by specifically modulating the NF-kappa B pathway in a MAP kinase-independent fashion.

L5 ANSWER 18 OF 45 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 2000115874 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10648614
TITLE: NF-kappaB activation by double-stranded-RNA-activated protein kinase (PKR) is mediated through NF-kappaB-inducing kinase and IkappaB kinase.
AUTHOR: Zamanian-Daryoush M; Mogensen T H; DiDonato J A; Williams B R
CORPORATE SOURCE: Department of Cancer Biology, The Lerner Research Institute, The Cleveland Clinic Foundation, Cleveland, Ohio 44195, USA.
CONTRACT NUMBER: AI34039 (United States NIAID)
SOURCE: Molecular and cellular biology, (2000 Feb) Vol. 20, No. 4, pp. 1278-90.
Journal code: 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal, Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 29 Feb 2000
Last Updated on STN: 20 Apr 2002
Entered Medline: 15 Feb 2000

AB The interferon (IFN)-inducible double-stranded-RNA (dsRNA)-activated serine-threonine protein kinase (PKR) is a major mediator of the antiviral and antiproliferative activities of IFNs. PKR has been implicated in different stress-induced signaling pathways including dsRNA signaling to nuclear factor kappa B (NF-kappaB). The mechanism by which PKR mediates activation of NF-kappaB is unknown. Here we show that in response to poly(rI). poly(rC) (pIC), PKR activates IkappaB kinase (IKK), leading to the degradation of the inhibitors IkappaBalpha and IkappaBbeta and the concomitant release of NF-kappaB. The results of kinetic studies revealed that pIC induced a slow and prolonged activation of IKK, which was preceded by PKR activation. In PKR null cell lines, pIC failed to stimulate IKK activity compared to cells from an isogenic background wild type for PKR in accord with the inability of PKR null cells to induce NF-kappaB in response to pIC. Moreover, PKR was required to establish a sustained response to tumor necrosis factor alpha (TNF-alpha) and to potentiate activation of NF-kappaB by cotreatment with TNF-alpha and IFN-gamma. By coimmunoprecipitation, PKR was shown to be physically associated with the IKK complex. Transient expression of a dominant negative mutant of IKKbeta or the NF-kappaB-inducing kinase (NIK) inhibited pIC-induced gene expression from an NF-kappaB-dependent reporter construct. Taken together, these results demonstrate that PKR-dependent dsRNA induction of NF-kappaB is mediated by NIK and IKK activation.

L5 ANSWER 19 OF 45 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 1999329013 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10400625
TITLE: c-E10 is a caspase-recruiting domain-containing protein that interacts with components of death receptors signaling

pathway and activates nuclear factor-kappaB.
 AUTHOR: Costanzo A; Guiet C; Vito P
 CORPORATE SOURCE: Fondazione A. Cesalpino, I Clinica Medica, V.le Policlinico
 155, 00161 Roma, Italy.
 SOURCE: The Journal of biological chemistry, (1999 Jul 16)
 Vol. 274, No. 29, pp. 20127-32.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 OTHER SOURCE: GENBANK-AF105066
 ENTRY MONTH: 199908
 ENTRY DATE: Entered STN: 27 Aug 1999
 Last Updated on STN: 27 Aug 1999
 Entered Medline: 19 Aug 1999

AB Members of the tumor necrosis factor receptor superfamily induce apoptosis
 via interaction with FADD and regulate cell growth and differentiation
 through TRADD and TRAFs molecules. While screening for molecules involved
 in the regulation of death receptor signaling, we identified a novel
 protein, c-E10. c-E10 contains an amino-terminal caspase-recruiting domain
 (CARD) and shares a sequence homologous with E10, a viral CARD-containing
 protein that binds to c-E10. In transfection experiments c-E10
 oligomerizes, binds to the cytoplasmic portion of TRAIL receptor 1 (DR4)
 and coprecipitates with TRADD. Expression of c-E10 under the
 control of a doxycycline-dependent transcriptional transactivator results
 in NF-kappaB activation, which is inhibited by dominant negative
 forms of TRAF2 and NIK kinase. Thus, our results suggest that
 c-E10 is an adapter protein that activates NF-kappaB through a molecular
 pathway involved in death receptor signaling.

L5 ANSWER 20 OF 45 MEDLINE on STN DUPLICATE 25
 ACCESSION NUMBER: 1999321931 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10391945
 TITLE: Differential IkappaB kinase activation and IkappaBalpha
 degradation by interleukin-1beta and tumor necrosis
 factor-alpha in human U937 monocytic cells. Evidence for
 additional regulatory steps in kappaB-dependent
 transcription.

AUTHOR: Nasuhara Y; Adcock I M; Catley M; Barnes P J; Newton R
 CORPORATE SOURCE: Department of Thoracic Medicine, National Heart and Lung
 Institute, Imperial College School of Medicine, London SW3
 6LY, United Kingdom.
 SOURCE: The Journal of biological chemistry, (1999 Jul 9)
 Vol. 274, No. 28, pp. 19965-72.
 Journal code: 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199908
 ENTRY DATE: Entered STN: 16 Aug 1999
 Last Updated on STN: 19 Sep 2002
 Entered Medline: 5 Aug 1999

AB The IkappaB kinases (IKKs) lie downstream of the NF-kappaB-inducing kinase
 (NIK) and activate NF-kappaB by phosphorylation of IkappaBalpha. This
 leads to IkappaBalpha degradation and release of NF-kappaB. In U937
 monocytic cells, interleukin (IL)-1beta (1 ng/ml) and tumor necrosis
 factor (TNF)-alpha; 10 ng/ml induced kappaB-dependent transcription
 equally. However, IKK activity was strongly induced by TNF-alpha but not

by IL-1beta. This was consistent with IkappaBalpha phosphorylation and degradation, yet TNF-alpha-induced NF-kappaB DNA binding was only 30-40% greater than for IL-1beta. This was not explained by degradation of IkappaBbeta, IkappaBepsilon, or p105 nor nuclear translocation of NF-kappaB. IkappaBalpha complexes or degradation-independent release of NF-kappaB. Dominant negative (NIK) repressed TNF-alpha and IL-1beta-induced kappaB-dependent transcription by approximately 60% and approximately 35%, respectively. These data reveal an imprecise relationship between IKK activation, IkappaBalpha degradation, and NF-kappaB DNA binding, suggesting the existence of additional mechanisms that regulate NF-kappaB activation. Finally, the lack of correlation between DNA binding and transcriptional activation plus the fact that PP1 and genistein both inhibited kappaB-dependent transcription without affecting DNA binding activity demonstrate the existence of regulatory steps downstream of NF-kappaB DNA binding. Therapeutically these data are important as inhibition of the NIK-IKK-IkappaBalpha cascade may not produce equivalent reductions in NF-kappaB-dependent gene expression.

L5	ANSWER 21 OF 45	MEDLINE on STN	DUPLICATE 26
ACCESSION NUMBER:	1999214545	MEDLINE	
DOCUMENT NUMBER:	PubMed ID: 10187770		
TITLE:	CIPER, a novel NF kappaB-activating protein containing a caspase recruitment domain with homology to Herpesvirus-2 protein E10.		
AUTHOR:	Koseki T; Inohara N; Chen S; Carrio R; Merino J; Hottiger M O; Nabel G J; Nunez G		
CORPORATE SOURCE:	Department of Pathology and Comprehensive Cancer Center, The University of Michigan Medical School, Ann Arbor, Michigan 48109, USA.		
CONTRACT NUMBER:	CA-64421 (United States NCI) CA-64556 (United States NCI)		
SOURCE:	The Journal of biological chemistry, (1999 Apr 9) Vol. 274, No. 15, pp. 9955-61. Journal code: 2985121R. ISSN: 0021-9258.		
PUB. COUNTRY:	United States		
DOCUMENT TYPE:	(COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)		
LANGUAGE:	English		
FILE SEGMENT:	Priority Journals		
OTHER SOURCE:	GENBANK-AF057700; GENBANK-AF057701		
ENTRY MONTH:	199905		
ENTRY DATE:	Entered STN: 17 May 1999 Last Updated on STN: 3 Mar 2000 Entered Medline: 3 May 1999		

AB We have identified and characterized CIPER, a novel protein containing a caspase recruitment domain (CARD) in its N terminus and a C-terminal region rich in serine and threonine residues. The CARD of CIPER showed striking similarity to E10, a product of the equine herpesvirus-2. CIPER formed homodimers via its CARD and interacted with viral E10 but not with several apoptosis regulators containing CARDS including ARC, RAIDD, RICK, caspase-2, caspase-9, or Apaf-1. Expression of CIPER induced NF-kappaB activation, which was inhibited by dominant-negative NIK and a nonphosphorylatable IkappaB-alpha mutant but not by dominant-negative RIP. Mutational analysis revealed that the N-terminal region of CIPER containing the CARD was sufficient and necessary for NF-kappaB-inducing activity. Point mutations in highly conserved residues in the CARD of CIPER disrupted the ability of CIPER to activate NF-kappaB and to form homodimers, indicating that the CARD is essential for NF-kappaB activation and dimerization. We propose that CIPER acts in a

NIK-dependent pathway of NF-kappaB activation.

L5 ANSWER 22 OF 45 MEDLINE on STN DUPLICATE 27
 ACCESSION NUMBER: 2000027389 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10557090
 TITLE: Inhibition of cyclo-oxygenase 2
 expression in colon cells by the chemopreventive
 agent curcumin involves inhibition of NF-kappaB
 activation via the NIK/IKK signalling complex.
 AUTHOR: Plummer S M; Holloway K A; Manson M M; Munks R J; Kaptein
 A; Farrow S; Howells L
 CORPORATE SOURCE: MRC Toxicology Unit, University of Leicester, Leicester,
 LE1 9HN, UK.
 SOURCE: Oncogene, (1999 Oct 28) Vol. 18, No. 44, pp.
 6013-20.
 Journal code: 8711562. ISSN: 0950-9232.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199912
 ENTRY DATE: Entered STN: 13 Jan 2000
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 3 Dec 1999

AB Colorectal cancer is a major cause of cancer deaths in Western countries,
 but epidemiological data suggest that dietary modification might reduce
 these by as much as 90%. Cyclo-oxygenase 2 (COX2), an inducible isoform
 of prostaglandin H synthase, which mediates prostaglandin synthesis during
 inflammation, and which is selectively overexpressed in colon tumours, is
 thought to play an important role in colon carcinogenesis. Curcumin, a
 constituent of turmeric, possesses potent anti-inflammatory activity and
 prevents colon cancer in animal models. However, its mechanism of action
 is not fully understood. We found that in human colon epithelial cells,
 curcumin inhibits COX2 induction by the colon tumour promoters, tumour
 necrosis factor alpha or fecapentaene-12. Induction of COX2 by
 inflammatory cytokines or hypoxia-induced oxidative stress can be mediated
 by nuclear factor kappa B (NF-kappaB). Since curcumin inhibits NF-kappaB
 activation, we examined whether its chemopreventive activity is related to
 modulation of the signalling pathway which regulates the stability of the
 NF-kappaB-sequestering protein, IkappaB. Recently components of this
 pathway, NF-kappaB-inducing kinase and IkappaB kinases, IKKalpha and beta,
 which phosphorylate IkappaB to release NF-kappaB, have been characterised.
 Curcumin prevents phosphorylation of IkappaB by inhibiting the activity of
 the IKKs. This property, together with a long history of consumption
 without adverse health effects, makes curcumin an important candidate for
 consideration in colon cancer prevention.

L5 ANSWER 23 OF 45 MEDLINE on STN DUPLICATE 28
 ACCESSION NUMBER: 1999315915 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10385526
 TITLE: The zinc finger protein A20 inhibits TNF-induced
 NF-kappaB-dependent gene expression by interfering with an
 RIP- or TRAF2-mediated transactivation signal and directly
 binds to a novel NF-kappaB-inhibiting protein ABIN.
 AUTHOR: Heynrick K; De Valck D; Vanden Berghe W; Van Crielinge W;
 Contreras R; Fiers W; Haegeman G; Beyaert R
 CORPORATE SOURCE: Department of Molecular Biology, Flanders Interuniversity
 Institute for Biotechnology, University of Ghent, B-9000
 Ghent, Belgium.
 SOURCE: The Journal of cell biology, (1999 Jun 28) Vol.
 145, No. 7, pp. 1471-82.

Journal code: 0375356. ISSN: 0021-9525.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals; AIDS
 OTHER SOURCE: GENBANK-AJ242777; GENBANK-AJ242778
 ENTRY MONTH: 199908
 ENTRY DATE: Entered STN: 16 Aug 1999
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 2 Aug 1999

AB The zinc finger protein A20 is a tumor necrosis factor (TNF)- and interleukin 1 (IL-1)-inducible protein that negatively regulates nuclear factor-kappa B (NF-kappaB)-dependent gene expression. However, the molecular mechanism by which A20 exerts this effect is still unclear. We show that A20 does not inhibit TNF- induced nuclear translocation and DNA binding of NF-kappaB, although it completely prevents the TNF- induced activation of an NF-kappaB-dependent reporter gene, as well as TNF-induced IL-6 and granulocyte macrophage-colony stimulating factor gene expression. Moreover, NF-kappaB activation induced by overexpression of the TNF receptor-associated proteins TNF receptor-associated death domain protein (TRADD), receptor interacting protein (RIP), and TNF receptor-associated factor 2 (TRAF2) was also inhibited by expression of A20, whereas NF-kappaB activation induced by overexpression of NF-kappaB-inducing kinase (NIK) or the human T cell leukemia virus type 1 (HTLV-1) Tax was unaffected. These results demonstrate that A20 inhibits NF-kappaB-dependent gene expression by interfering with a novel TNF-induced and RIP- or TRAF2-mediated pathway that is different from the NIK-IkappaB kinase pathway and that is specifically involved in the transactivation of NF-kappaB. Via yeast two-hybrid screening, we found that A20 binds to a novel protein, ABIN, which mimics the NF-kappaB inhibiting effects of A20 upon overexpression, suggesting that the effect of A20 is mediated by its interaction with this NF-kappaB inhibiting protein, ABIN.

L5 ANSWER 24 OF 45 MEDLINE on STN DUPLICATE 29
 ACCESSION NUMBER: 1999098989 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9882303
 TITLE: Epstein-Barr virus-encoded latent membrane protein 1 activates the JNK pathway through its extreme C terminus via a mechanism involving TRADD and TRAF2.
 AUTHOR: Eliopoulos A G; Blake S M; Floettmann J E; Rowe M; Young L S
 CORPORATE SOURCE: CRC Institute for Cancer Studies, The University of Birmingham Medical School, Birmingham B15 2TA, England.
 SOURCE: Journal of virology, (1999 Feb) Vol. 73, No. 2, pp. 1023-35.
 Journal code: 0113724. ISSN: 0022-538X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199902
 ENTRY DATE: Entered STN: 1 Mar 1999
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 18 Feb 1999

AB The transforming Epstein-Barr virus-encoded latent membrane protein 1 (LMP1) activates signalling on the NF-kappaB axis through two distinct domains in its cytoplasmic C terminus, namely, CTAR1 (amino acids [aa] 187 to 231) and CTAR2 (aa 351 to 386). The ability of CTAR1 to activate NF-kappaB appears to be attributable to the direct interaction of tumor

necrosis factor (TNF) receptor-associated factor 2 (TRAF2), while recent work indicates that CTAR2-induced NF-kappaB is mediated through its association with TNF receptor-associated death domain (TRADD). LMP1 expression also results in activation of the c-Jun N-terminal kinase (JNK) (also known as stress-activated protein kinase) cascade, an effect which is mediated exclusively through CTAR2 and can be dissociated from NF-kappaB induction. The organization and signalling components involved in LMP1-induced JNK activation are not known. In this study we have dissected the extreme C terminus of LMP1 and have identified the last 8 aa of the protein (aa 378 to 386) as being important for JNK signalling. Using a series of fine mutants in which single amino acids between codons 379 and 386 were changed to glycine, we have found that mutations of Pro379, Glu381, Ser383, or Tyr384 diminish the ability of LMP1 CTAR2 to engage JNK signalling. Interestingly, this region was also found to be essential for CTAR2-mediated NF-kappaB induction and coincides with the LMP1 amino acid sequences shown to bind TRADD. Furthermore, we have found that LMP1-mediated JNK activation is synergistically augmented by low levels of TRADD expression, suggesting that this adapter protein is critical for LMP1 signalling. TRAF2 is known to associate with TRADD, and expression of a dominant-negative N-terminal deletion TRAF2 mutant was found to partially inhibit LMP1-induced JNK activation in 293 cells. In addition, the TRAF2-interacting protein A20 blocked both LMP1-induced JNK and NF-kappaB activation, further implicating TRAF2 in these phenomena. While expression of a kinase-inactive mutated NF-kappaB-inducing kinase (NIK), a mitogen-activated protein kinase kinase kinase which also associates with TRAF2, impaired LMP1 signalling on the NF-kappaB axis, it did not inhibit LMP1-induced JNK activation, suggesting that these two pathways may bifurcate at the level of TRAF2. These data further define a role for TRADD and TRAF2 in JNK activation and confirm that LMP1 utilizes signalling mechanisms used by the TNF receptor/CD40 family to elicit its pleiotropic activities.

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 17:16:47 ON 24 SEP 2008

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L1      0 S SIRNA (S) NIK AND PD<=20041130
L2      17 S RNA (S) NIK AND PD<=20041130
L3      9 DUP REM L2 (8 DUPLICATES REMOVED)
L4      114 S EXPRESSION (S) (DOWN-REGULAT? OR INHIBIT?) (S) (NIK OR (NF-KA
L5      45 DUP REM L4 (69 DUPLICATES REMOVED)

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=> D Ibib abs L5 25-45

L5 ANSWER 25 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN

ACCESSION NUMBER: 2005:476356 BIOSIS

DOCUMENT NUMBER: PREV200510268260

TITLE: Rituximab-mediated inhibition of the constitutive NIK/IKK/I
kappa B/NF-kappa B signaling pathway in non-Hodgkin's
lymphoma (NHL) B-cell lines: Role in chemo-sensitization.

AUTHOR(S): Jazirehi, Ali R. [Reprint Author]; Huerta-Yepez, Sara;
Cheng, Genhong; Bonavida, Benjamin

CORPORATE SOURCE: Univ Calif Los Angeles, Los Angeles, CA USA

SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1,
pp. 86A.

Meeting Info.: 46th Annual Meeting of the
American-Society-of-Hematology. San Diego, CA, USA.
December 04 -07, 2004. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 16 Nov 2005

Last Updated on STN: 16 Nov 2005

AB The chimeric anti-CD20 antibody rituximab (Rituxan, IDEC-C2B8) is widely
used in the clinical treatment of patients with non-Hodgkin's lymphoma
(NHL). Rituximab sensitizes NHL B-cell lines to drug-induced apoptosis
via selective down-regulation of Bcl-(xL) expression (Jazirehi et al.,
Mol. Cancer Therapeutics 2:1183, 2003). We hypothesized that
rituximab-mediated down-regulation of Bcl-(xL) expression may be due, in
part, to inhibition of constitutive NF-kappa B activity that regulates
Bcl-(XL) expression. This hypothesis was tested following treatment with
rituximab of CD20+ drug-resistant Ramos (Bcl-2(-)/ Bcl-(+)(xK)) and Daudi
(Bcl-2(+)/ Bcl-(+)(xK)) cell lines. Rituximab decreased the
phosphorylation of NIK, IKK and I kappa B-alpha, diminished IKK kinase
activity and decreased NF-kappa B DNA-binding activity. These events and
down-regulation of Bcl-(xL) expression occurred with similar kinetics and
were observed 3-6 h post rituximab treatment. The role of NF-kappa B in
the regulation of Bcl-(xL) transcription in both Ramos and Daudi cells was
demonstrated by using 1) promoter reporter assays in which deletion of the
two tandem NF-kappa B binding sites in the upstream promoter region
significantly reduced the luciferase activity 2) I kappa B super-repressor
expressing cells and 3) by NF-kappa B specific inhibitors. The underlying
mechanism of the inhibition of the NF-kappa B signaling pathway
by rituximab was shown to be due, in part, to upregulation of Raf-1 kinase
inhibitor protein (RKIP) expression, thus, interrupting
the NF-kappa B signaling pathway through the physical association between
NIK and RKIP, which was concomitant with Bcl-(xL) down-

regulation. The direct role of Bcl-(xL) in drug-resistance was evaluated by using Bcl-(xL) over-expressing Ramos cells, which exhibited higher resistance to drugs that was partially reversed by rituximab. These findings reveal a novel mechanism of action of rituximab-mediated signaling by inducing RKIP expression that negatively regulates the constitutive NF-kappa B pathway resulting in Bcl-(xL) down-regulation and chemosensitization of the NHLB-cells. Furthermore, these findings identify several targets, namely RKIP, Bcl-(xL) and the components of the NF-kappa B signaling pathway, for therapeutic intervention in combination with cytotoxic agents to reverse adaptive. and acquired resistance of B-NHL.

L5 ANSWER 26 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:7452 BIOSIS
DOCUMENT NUMBER: PREV200400008383
TITLE: Inhibitor of the inflammatory response induced by TNFalpha and IL-1.
AUTHOR(S): Greene, Warner C. [Inventor, Reprint Author]; Lin, Xin [Inventor]; Gelezuinas, Romas [Inventor]
CORPORATE SOURCE: ASSIGNEE: The Regents of the University of California
PATENT INFORMATION: US 6645728 20031111
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Nov 11 2003) Vol. 1276, No. 2.
<http://www.uspto.gov/web/menu/patdata.html>. e-file.
ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Dec 2003
Last Updated on STN: 17 Dec 2003
AB The present invention provides the molecular basis for cytokine induction of NF-kappaB-dependent immune and inflammatory responses, emphasizing a role for both NIK-NIK and NIK-IKK protein--protein interactions. A relatively small region of NIK selectively impairs the NIK-IKK interaction. The present invention provides a novel and highly specific method for modulating NF-kappaB-dependent immune, inflammatory, and anti-apoptotic responses, based on interruption of the critical protein--protein interaction of NIK and IKK. The present invention provides methods for inhibiting NF-kappaB-dependent gene expression, using mutant NIK proteins. One embodiment of the present invention provides kinase-deficient NIK mutant proteins that inhibit activation of IKK. Another embodiment of the invention provides N-terminus NIK mutant proteins that bind IKK, thus inhibiting NIK/IKK interaction.

L5 ANSWER 27 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:582358 BIOSIS
DOCUMENT NUMBER: PREV200300572193
TITLE: PROTEIN KINASE C-DELTA PLAYS A PIVOTAL ROLE IN GASTRIN-INDUCED ACTIVATION OF NF-kappaB IN GASTRIC EPITHELIAL CELLS
AUTHOR(S): Toyota, Miyuki [Reprint Author]; Miyazaki, Yoshiji [Reprint Author]; Kishida, Osamu [Reprint Author]; Miyazaki, Tamana [Reprint Author]; Tsutsui, Shusaku [Reprint Author]; Kiyohara, Tatsuya [Reprint Author]; Shinomura, Yasuhisa [Reprint Author]; Matsuzawa, Yuji [Reprint Author]
CORPORATE SOURCE: Osaka, Japan
SOURCE: Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. T1017. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of

Liver Diseases; American Gastroenterological Association;
American Society for Gastrointestinal Endoscopy; Society
for Surgery of the Alimentary Tract.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Background & Aims: We previously reported that gastrin is capable of activating NF-kappaB through a protein kinase C (PKC)-dependent pathway in gastric epithelial cells. The present study was performed to determine which PKC isozyme is involved in gastrin receptor-mediated signals leading to activation of NF-kappaB. Methods: The cells used in the present study were MKGR26 cells created by transfecting gastrin receptor cDNA into MKN-28 gastric cancer cells and guinea pig isolated parietal cells. Phosphorylated PKC- γ was detected by Western blot analysis. NF-kappaB transcriptional activity and binding activity were determined by luciferase assay using the pNF-kappaB-LUC containing five copies of consensus NF-kappaB site linked to a minimal E1B promoter-luciferase reporter gene and electrophoretic mobility shift analysis respectively. Results: Gastrin induced activation of NF-kappaB in both MKGR26 cells and isolated parietal cells. The general PKC inhibitor GF109203X and rottlerin, an inhibitor of PKC- α and PKC- θ , inhibited gastrin-induced DNA-protein complex formation in MKN-28 cells and guinea pig isolated parietal cells, while HBDDE, an inhibitor of PKC- α and PKC- γ , had no effect on the complex formation. Rottlerin also inhibited the gastrin-induced transcriptional activity of NF-kappaB in MKGR26 cells, while Go6976, an inhibitor of PKC- α and PKC- β , had no effect on this process. Introduction of the dominant negative PKC- δ into MKGR26 cells abrogated gastrin-stimulated NF-kappaB activation, while the dominant negative PKC- θ had no effect. Gastrin induced phosphorylation of PKC- δ in MKGR26 cells within 5 minutes and the phosphorylation remained for over 60 minutes. Forced expression of wild-type PKC- δ alone induced NF-kappaB activation in MKGR26 cells, which was inhibited by co-transfection of the dominant negative mutant of TRAF6, NIK or IKKs. Conclusions: PKC δ plays a pivotal role in gastrin-induced activation of NF-kappaB in gastric epithelial cells..

L5 ANSWER 28 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:431940 BIOSIS

DOCUMENT NUMBER: PREV200200431940

TITLE: Lipopolysaccharide induction of cyclooxygenase-2 expression is mediated via mitogen-activated protein kinase and nuclear factor-kB pathways in canine tracheal smooth muscle cells.

AUTHOR(S): Yang, Chuen-Mao [Reprint author]

CORPORATE SOURCE: Pharmacology, Chang Gung University, 259 Wen-Hwa 1 Road Kwei-San, Tao-Yuan, 3332, Taiwan

SOURCE: FASEB Journal, (March 22, 2002) Vol. 16, No. 5, pp. A1147. print.
Meeting Info.: Annual Meeting of Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Aug 2002
Last Updated on STN: 14 Aug 2002

AB Lipopolysacchride (LPS) was found to induce inflammatory responses in the airways through PG synthesis. This study was to determine the mechanism of LPS-enhanced COX-2 expression associated with PGE2 synthesis in TSMCs. LPS increased COX-2 expression and PGE2 formation in a time- and concentration-dependent manner. COX-2 expression and PGE2 formation in response to LPS were attenuated by genistein, D609, U73122, GF109203X, staurosporine, removal of Ca2+ by addition of BAPTA/AM plus EGTA, LY294002, and wortmannin. Furthermore, LPS-induced activation of NF-kB correlated with the degradation of Ikb-alpha in TSMCs. LPS-induced NF-kB activation, COX-2 expression, and PGE2 synthesis was inhibited by the dominant negative mutants of NIK and IKK-alpha, but not by IKK-beta. LPS-induced COX-2 expression and PGE2 synthesis were completely inhibited by PD98059 and SB203580, but these two inhibitors had no effect on LPS)-induced NF-kB activation, indicating that activation of p42/44 and p38 MAPK and NF-kB signaling pathways were independently required for these responses. These findings suggest that the increased expression of COX-2 correlates with the release of PGE2 from LPS-challenged TSMCs, at least in part, independently mediated through MAPKs and NF-kB signaling pathways in canine TSMCs. IL-1beta-mediated responses were modulated by PLC, Ca2+, PKC, tyrosine kinase, and PI3-K in these cells.

L5 ANSWER 29 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:447244 BIOSIS
DOCUMENT NUMBER: PREV200100447244
TITLE: Inhibitor of the inflammatory response induced by the TNFA and IL-1.
AUTHOR(S): Greene, Warner C. [Inventor]; Lin, Xin [Inventor, Reprint author]; Gelezuinas, Romas [Inventor]
CORPORATE SOURCE: San Francisco, CA, USA
ASSIGNEE: The Regents of the University of California
PATENT INFORMATION: US 6265538 20010724
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (July 24, 2001) Vol. 1248, No. 4. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2001
Last Updated on STN: 22 Feb 2002

AB The present invention provides the molecular basis for cytokine induction of NF-kappaB-dependent immune and inflammatory responses, emphasizing a role for both NIK-NIK and NIK-IKK protein-protein interactions. A relatively small region of NIK selectively impairs the NIK-IKK interaction. The present invention provides a highly specific method for modulating NF-kappaB-dependent immune, inflammatory, and anti-apoptotic responses, based on interruption of the critical protein-protein interaction of NIK and IKK. The present invention provides methods for inhibiting NF-kappaB-dependent gene expression, using mutant NIK proteins. One embodiment of the present invention provides kinase-deficient NIK mutant proteins that inhibit activation of IKK. Another embodiment of the invention provides N-terminus NIK mutant proteins that bind IKK, thus inhibiting NIK/IKK interaction.

L5 ANSWER 30 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:244372 BIOSIS
DOCUMENT NUMBER: PREV200100244372
TITLE: The rotavirus VP4 protein directs cellular transcription by engaging a TRAF2-NIK signaling pathway.
AUTHOR(S): Mackow, Erich R. [Reprint author]; Kocer, Salih [Reprint

author]; Geimonen, Erika [Reprint author]; LaMonica, Rachel
CORPORATE SOURCE: HSC, SUNY at Stony Brook, T17 Rm048, Stony Brook, NY,
11794-8173, USA
SOURCE: FASEB Journal, (March 8, 2001) Vol. 15, No. 5,
pp. A907. print.
Meeting Info.: Annual Meeting of the Federation of American
Societies for Experimental Biology on Experimental Biology
2001. Orlando, Florida, USA. March 31-April 04, 2001.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2001
Last Updated on STN: 19 Feb 2002
AB Rotaviruses rapidly activate NF-kappaB and induce chemokine secretion
following infection of intestinal epithelial cells (IECs). In IECs,
NF-kappaB activation is effected through cytoplasmic signaling pathways
requiring TNF Receptor Associated Factor 2 (TRAF2) (1). The ability of
rotavirus particles which lack genomic RNA to activate NF-kappaB suggested
that protein components of the rotavirus virion could direct cellular
signaling. The rotavirus capsid protein VP4, and its' N-terminal VP8*
cleavage product, contains TRAF binding motifs which are conserved among
rotaviruses and only present in viral VP4 proteins. We have determined
that cellular TRAFs (1, 2 and 3) are bound by the rhesus rotavirus (RRV)
VP8* protein through three discrete TRAF-binding domains. Expression of
either VP4 or VP8* selectively induces a 5-7 fold increase in NF-kappaB
activity and synergistically enhances TRAF2 mediated NF-kappaB activation.
Mutagenesis of VP8* TRAF binding motifs abolished VP8* binding to TRAFs
and the ability of the protein to activate NF-kappaB. Expression
of pathway specific dominant negative (DN) inhibitors, DN-TRAF2
or DN-NF-kappaB Inducing Kinase (DN-NIK), also abolished VP8*-,
VP4- or rotavirus-mediated NF-kappaB activation. These findings
demonstrate that rotavirus primarily activates NF-kappaB through a
TRAF2-NIK signaling pathway and that VP4 and VP8* direct pathway
activation through interactions with cellular TRAFs. Additional
transcriptional reporters (AP-1, SRE and CRE) were not activated by VP8*
or rotavirus infection suggesting that rotaviruses selectively elicit
NF-kappaB-directed transcriptional responses. These results establish
that fully cytoplasmic rotaviruses regulate cellular transcription by
selectively engaging a TRAF2 signaling pathway of NF-kappaB activation.
This suggests that rotaviruses direct specific cellular responses which
could contribute to viral pathogenesis or host immunity.

L5 ANSWER 31 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on
STN
ACCESSION NUMBER: 2001:525188 BIOSIS
DOCUMENT NUMBER: PREV200100525188
TITLE: Hydrogen peroxide-mediated inhibition of
lipopolysaccharide-stimulated inhibitory kappa B kinase
activity in rat aortic smooth muscle cells.
AUTHOR(S): Torrie, Lindsay J.; MacKenzie, Christopher J.; Paul,
Andrew; Plevin, Robin [Reprint author]
CORPORATE SOURCE: Department of Physiology and Pharmacology, Strathclyde
Institute for Biomedical Sciences, University of
Strathclyde, 27 Taylor Street, Glasgow, G4 0NR, UK
r.plevin@strath.ac.uk
SOURCE: British Journal of Pharmacology, (September, 2001
) Vol. 134, No. 2, pp. 393-401. print.
CODEN: BJPCBM. ISSN: 0007-1188.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Nov 2001

Last Updated on STN: 23 Feb 2002

AB 1 In rat aortic smooth muscle cells (RASMC), exposure to lipopolysaccharide (LPS) resulted in NF-kappaB-DNA binding, degradation of IkappaB-alpha, -beta and -epsilon and increased activity of both alpha and beta isoforms of inhibitory kappa B kinase (IKK). 2 Expression of dominant-negative (DN)-IKK-alpha, IKK-beta and NF-kappaB-inducing kinase (NIK) abolished LPS-stimulated NF-kappaB reporter activity, suggesting that activation of a NIK /IKK-dependent pathway is indispensable for NF-kappaB activation by LPS in this cell type. 3 The tyrosine phosphatase inhibitor, pervanadate, abolished LPS-stimulated NF-kappaB-DNA-binding activity. However, the effect of pervanadate was shown to be mediated by excess hydrogen peroxide (H2O2) present in the reaction mix. Preincubation of RASMC with H2O2 inhibited LPS-stimulated IKK kinase activity and downstream NF-kappaB-DNA binding activity. 4 H2O2 also strongly stimulated p38 MAP kinase activity in RASMCs. Effective inhibition of this pathway using SB203580 did not reverse the effects of H2O2 on LPS-stimulated IKK/NF-kappaB signalling. 5 These studies show that hydrogen peroxide-mediated inhibition of LPS-stimulated NF-kappaB activation in RASMC occurs upstream of IKK. The inhibitory effect of H2O2 is not due to tyrosine phosphatase inhibition, it is mediated by H2O2 through a mechanism which is independent of any cross-talk involving MAP kinase homologues.

L5 ANSWER 32 OF 45 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:336258 BIOSIS
DOCUMENT NUMBER: PREV199900336258
TITLE: Curcumin, a dietary product, blocks cytokine mediated NF-kappaB activation and proinflammatory gene expression in intestinal epithelial cells by inhibiting IKK activity without directly affecting NF-kappaB-inducing kinase (NIK) or IkgappaB kinase (IKK).
AUTHOR(S): Jobin, Christian [Reprint author]; Bradham, C. A. [Reprint author]; Narula, A. S. [Reprint author]; Brenner, D. A. [Reprint author]; Sartor, R. B. [Reprint author]
CORPORATE SOURCE: Univ of North Carolina, Chapel Hill, NC, USA
SOURCE: Gastroenterology, (April, 1999) Vol. 116, No. 4 PART 2, pp. A743. print.
Meeting Info.: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association. Orlando, Florida, USA. May 16-19, 1999. American Gastroenterological Association.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

L5 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:787970 CAPLUS
DOCUMENT NUMBER: 141:374550
TITLE: Inhibition of ICAM-1 gene expression, monocyte adhesion and cancer cell invasion by targeting IKK complex: molecular and functional study of novel alpha-methylene-gamma-butyrolactone derivatives
AUTHOR(S): Huang, Wei-Chien; Chan, Shu-Ting; Yang, Tzu-Lin; Tzeng, Cherng-Chyi; Chen, Ching-Chow
CORPORATE SOURCE: Department of Pharmacology, College of Medicine, National Taiwan University, Taipei, 10018, Taiwan

SOURCE: Carcinogenesis (2004), 25(10), 1925-1934
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The transcription factor nuclear factor-kappaB (NF- κ B) is a regulator related to cellular inflammation, immune responses and carcinogenesis. Therefore, components of the NF- κ B-activating signaling pathways are frequent targets for the anti-inflammatory and anticancer agents. In this study, CYL-19 s and CYL-26z, two synthetic α -methylene- γ -butyrolactone derivs., were shown to inhibit the tumor necrosis factor- α (TNF- α)-induced intercellular adhesion mol.-1 (ICAM-1) expression in human A549 alveolar epithelial cells and the adhesion of U937 cells to these cells. RT-PCR anal. also demonstrated their inhibitory effects on TNF- α -induced ICAM-1 mRNA expression. TNF- α -induced ICAM-1 and NF- κ B-dependent promoter activities were attenuated by CYL-19 s and CYL-26z. ICAM-1 promoter activities induced by the over-expression of wild-type NF- κ B-inducing kinase and I κ B kinase β (IKK β) were also inhibited by both compds. Furthermore, CYL-19 s and CYL-26z inhibited the TNF- α -induced phosphorylation and degradation of I κ B α and NF- κ B-specific DNA-protein binding activity via targeting IKK complex directly, without any effect on the activations of other kinases such as ERK1/2 and p38. In addition to ICAM-1 expression, CYL-19 s and CYL-26z also suppressed other NF- κ B-mediated gene expressions such as matrix metalloproteinase-9 (MMP-9) mRNA and cyclooxygenase-2 (COX-2) protein. In Matrigel assays, ICAM-1 and COX-2 expressions induced by TNF- α elicited A549 and NCI-H292 cell invasion, resp., and these effects were inhibited by both compds. In summary, our data demonstrated that CYL-19 s and CYL-26z down-regulate the TNF- α -induced inflammatory genes expression through suppression of IKK activity and NF- κ B activation. These agents may be effective in the anti-inflammatory and anticancer therapy.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2004:714326 CAPLUS
DOCUMENT NUMBER: 141:378789

TITLE: Role of NF- κ B and p38 MAP Kinase Signaling Pathways in the Lipopolysaccharide-Dependent Activation of Heme Oxygenase-1 Gene Expression
AUTHOR(S): Wijayanti, Nastiti; Huber, Sebastian; Samoylenko, Anatoly; Kietzmann, Thomas; Immenschuh, Stephan
CORPORATE SOURCE: Institut fuer Klinische Chemie und Pathobiochemie, Justus-Liebig-Universitaet Giessen, Giessen, D-35392, Germany

SOURCE: Antioxidants & Redox Signaling (2004), 6(5), 802-810
CODEN: ARSIF2; ISSN: 1523-0864

PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Heme oxygenase (HO)-1 is the inducible isoform of the rate-limiting enzyme of heme degradation, which is up-regulated by a host of stress stimuli. The bacterial cell membrane component lipopolysaccharide (LPS) is a prototypical activator of monocytic cells. Here, it is shown that LPS induced the endogenous HO-1 gene expression in RAW264.7 monocytic cells. To investigate the mol. mechanisms of HO-1 gene induction by LPS, the authors performed transfection expts. with reporter gene constructs containing sequences of the proximal rat HO-1 gene promoter. Deletion and mutation

anal. indicated that a cAMP response element/activator protein-1 site (-664/-657), but not an E-box motif (-47/-42), played a major role for LPS-dependent HO-1 gene induction. Up-regulation of HO-1 promoter activity by LPS was decreased by pharmacol. nuclear factor- κ B (NF- κ B) inhibitors and by cotransfected expression vectors with dominant neg. isoforms of NF- κ B-inducing kinase, inhibitor of NF- κ B (I κ B) kinase β , and I κ B α . Moreover, the p38 mitogen-activated protein kinase (MAPK) inhibitor SB203580 and overexpressed dominant neg. p38 β decreased, whereas dominant neg. p38 δ increased, LPS-dependent induction of HO-1 gene expression. The results suggest that the NF- κ B and p38 MAPK signaling pathways mediate the LPS-dependent induction of HO-1 gene expression via DNA sequences of the proximal promoter region.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 2003:613793 CAPLUS

DOCUMENT NUMBER: 140:52924

TITLE: Ursolic acid inhibits nuclear factor- κ B activation induced by carcinogenic agents through suppression of I κ B α kinase and p65 phosphorylation: correlation with down-regulation of cyclooxygenase 2, matrix metalloproteinase 9, and cyclin D1

AUTHOR(S): Shishodia, Shishir; Majumdar, Sekhar; Banerjee, Sanjeev; Aggarwal, Bharat B.

CORPORATE SOURCE: Department of Bioimmunotherapy, Cytokine Research Laboratory, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Cancer Research (2003), 63(15), 4375-4383
CODEN: CNREAS; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The process of tumorigenesis requires cellular transformation, hyperproliferation, invasion, angiogenesis, and metastasis. Several genes that mediate these processes are regulated by the transcription factor nuclear factor- κ B (NF- κ B). The latter is activated by various carcinogens, inflammatory agents, and tumor promoters. Thus, agents that can suppress NF- κ B activation have the potential to suppress carcinogenesis. Ursolic acid, a pentacyclic triterpene acid, has been shown to suppress the expression of several genes associated with tumorigenesis, but whether ursolic acid mediates its effects through suppression of NF- κ B is not understood. In the study described in the present report, we found that ursolic acid suppressed NF- κ B activation induced by various carcinogens including tumor necrosis factor (TNF), phorbol ester, okadaic acid, H₂O₂, and cigarette smoke. These effects were not cell type specific. Ursolic acid inhibited DNA binding of NF- κ B consisting of p50 and p65. Ursolic acid inhibited I κ B α degradation, I κ B α phosphorylation, I κ B α kinase activation, p65 phosphorylation, p65 nuclear translocation, and NF- κ B-dependent reporter gene expression. Ursolic acid also inhibited NF- κ B-dependent reporter gene expression activated by TNF receptor, TNF receptor-associated death domain, TNF receptor-associated factor, NF- κ B-inducing kinase, I κ B α kinase, and p65. The inhibition of NF- κ B activation correlated with suppression of NF- κ B-dependent cyclin D1, cyclooxygenase 2, and matrix metalloproteinase 9 expression. Thus, overall, our results indicate that ursolic acid inhibits I κ B α kinase and p65

phosphorylation, leading to the suppression of NF- κ B activation induced by various carcinogens. These actions of ursolic acid may mediate its antitumorigenic and chemosensitizing effects.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 2003:321568 CAPLUS

DOCUMENT NUMBER: 138:381120

TITLE: BRCAL splice variants exhibit overlapping and distinct transcriptional transactivation activities
AUTHOR(S): McEachern, Kristen A.; Archey, William B.; Douville, Karen; Arrick, Bradley A.

CORPORATE SOURCE: Departments of Biochemistry and Medicine, Dartmouth Medical School, Hanover, NH, 03755, USA

SOURCE: Journal of Cellular Biochemistry (2003), 89(1), 120-132
CODEN: JCEBD5; ISSN: 0730-2312

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The global changes in gene expression induced by transient increased expression of full length BRCAL as well as the spliced variant BRCALs were evaluated by cDNA expression array in a human non-tumorigenic mammary epithelial cell line, MCF10A. Over 30 genes were identified that displayed an altered expression pattern in response to the expression of BRCAL splice variants. The expression of NF- κ B inducing kinase was markedly down-regulated in BRCAL transfected cells. However, a NF- κ B-responsive promoter construct yielded increased basal activity in BRCAL transfected cells, as well as following treatment with tumor necrosis factor- α or lymphotoxin. In addition, nuclear exs. from BRCAL transfected cells displayed increased DNA binding to the κ B consensus site. The transcriptional activity of a panel of promoter constructs was evaluated following expression of wild type or mutant BRCAL. Full length BRCAL transactivated the estrogen receptor- α (ER α) and BCL2 promoters as well as AP-1, SRE, and CRE containing promoters. Transactivation activity of the exon 11-deleted BRCALs was more limited and usually of lower magnitude. The ability of a pathogenic mutation, 5382insC, to abrogate the transcriptional transactivation by BRCAL and BRCALs was also investigated. Mutant BRCAL retained wild type levels of transcriptional activity for the ER α promoter as well as for the NF- κ B, AP-1, and CRE-responsive promoters but had reduced or no activity with the BCL2 and SRE promoters. These results show that BRCAL isoforms have both overlapping and distinct transcriptional transactivation activity, and that a mutant form of BRCAL implicated in carcinogenesis is not devoid of all activity.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 17

ACCESSION NUMBER: 2001:436389 CAPLUS

DOCUMENT NUMBER: 135:191720

TITLE: VP4 differentially regulates TRAF2 signaling, disengaging JNK activation while directing NF- κ B to effect rotavirus-specific cellular responses
AUTHOR(S): LaMonica, Rachel; Kocer, Salih S.; Nazarova, Jennet; Dowling, William; Geimonen, Erika; Shaw, Robert D.; Mackow, Erich R.

CORPORATE SOURCE: Department of Medicine, Department of Molecular Genetics and Microbiology, State University of New York, Stony Brook, NY, 11794, USA

SOURCE: Journal of Biological Chemistry (2001),
276(23), 19889-19896
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rotaviruses rapidly activate NF- κ B and induce the secretion of
selected chemokines after infection. The ability of rotavirus particles
lacking genomic RNA to activate NF- κ B suggested that rotavirus
proteins direct cell signaling responses. We identified conserved
TNFR-associated factor (TRAF) binding motifs within the rotavirus capsid
protein VP4 and its N-terminal VP8* cleavage product. TRAFs (-1, -2, and
-3) are bound by the rhesus rotavirus VP8* protein through three discrete
TRAF binding domains. Expression of VP4 or VP8* from rhesus or human
rotaviruses induced a 5-7-fold increase in NF- κ B activity and
synergistically enhanced TRAF2-mediated NF- κ B activation.
Mutagenesis of VP8* TRAF binding motifs abolished VP8* binding to TRAFs
and the ability of the protein to activate NF- κ B.
Expression of pathway-specific dominant neg. (DN)
inhibitors DN-TRAF2 or DN-NF- κ B.
-inducing kinase also abolished VP8*-induced, VP4-, or
rotavirus-mediated NF- κ B activation. These findings demonstrate
that rotavirus primarily activates NF- κ B through a
TRAF2-NF- κ B-inducing kinase signaling pathway and that VP4 and VP8*
proteins direct pathway activation through interactions with cellular
TRAFs. In contrast, transcriptional responses from AP-1 reporters were
inhibited 5-fold by VP8* and were not activated by rotavirus infection,
suggesting the differential regulation of TRAF2 signaling responses by
VP8*. VP8* blocked JNK activation directed by TRAF2 or TRAF5 but had no
effect on JNK activation directed by TRAF6 or MEKK1. This establishes
that fully cytoplasmic rotaviruses selectively engage signaling pathways,
which regulate cellular transcriptional responses. These findings also
demonstrate that TRAF2 interactions can disengage JNK signaling from
NF- κ B activation and thereby provide a new means for TRAF2
interactions to determine pathway-specific responses.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:293778 CAPLUS

DOCUMENT NUMBER: 139:67556

TITLE: Human RPE-monocyte co-culture induces chemokine gene
expression through activation of MAPK and NIK cascade

AUTHOR(S): Bian, Zong-Mei; Elner, Susan G.; Yoshida, Ayako;
Elner, Victor M.

CORPORATE SOURCE: Department of Ophthalmology, University of Michigan,
Ann Arbor, MI, 48105, USA

SOURCE: Experimental Eye Research (2003), 76(5),
573-583
CODEN: EXERA6; ISSN: 0014-4835

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cell-cell contact between human retinal pigment epithelium (hRPE) cells
and monocytes occurs in many retinal diseases involving blood-retinal
barrier breakdown. This study investigates chemokine secretion induced by
co-culture of hRPE cells and monocytes and illustrates the roles of p38
kinase, ERK1, JNK/SAPK and NF- κ B-inducing kinase signaling pathways
for hRPE IL-8 and MCP-1 secretion induced in hRPE by co-culture with
monocytes. Co-culture of hRPE cells with monocytes increased steady-state
IL-8 and MCP-1 mRNA and protein secretion. Stimulation of hRPE cells by

monocytes resulted in prominent increases in p38, ERK1/2 and JNK/SAPK phosphorylation, I κ B degradation, and NF- κ B nuclear translocation. The induced IL-8 and MCP-1 proteins were almost completely suppressed by U0126, a specific mitogen-activated protein kinase kinase (MEK) inhibitor, or by SB203580, a selective p38 inhibitor. Chemokine secretion was completely blocked by simultaneous administration of U0126 and SB203580. Induction of IL-8 and MCP-1 was abrogated by Ro318220, an inhibitor of PKC, as well as by genistein or herbimycin A, inhibitors of PTK. In addition, anti-inflammatory drugs dexamethasone (DEX) and cyclosporin A (CSA) both blocked activation of JNKs/SAPK and the cell-cell contact induced production of hRPE IL-8 and MCP-1, while activation of p38 and ERK was only inhibited by DEX, but not by CSA. These results suggest that activation of DEX-sensitive, CSA-resistant MEK/ERK and p38 pathways, and activation of NF- κ B, PKC, and PTK are essential for IL-8 and MCP-1 expression by hRPE cells.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:114033 CAPLUS

DOCUMENT NUMBER: 136:178935

TITLE: Antisense oligonucleotides inhibiting expression of the gene for HPK/GCK-like kinase

INVENTOR(S): Dean, Nicholas M.; Cowser, Lex M.

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: U.S., 37 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6346416	B1	20020212	US 2000-651011	20000829 <--
WO 2002018409	A1	20020307	WO 2001-US25860	20010817 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG AU 2001083443 A 20020313 AU 2001-83443 20010817 <-- AU 2001083443 A 20020313 AU 2001-83443 20010817 <-- AU 2001083443 A 20020313 AU 2001-83443 20010817 <-- AU 2001083443 A 20020313 AU 2001-83443 20010817 <--				
PRIORITY APPLN. INFO.:				
AU 2001-83443 20010817 <-- US 2000-651011 A 20000829 WO 2001-US25860 W 20010817				

AB Antisense compds., compns. and methods are provided for modulating the expression of HPK/GCK-like kinase also known as NIK kinase. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding HPK/GCK-like kinase. Methods of using these compds. for modulation of HPK/GCK-like kinase expression and for treatment of diseases associated with expression of HPK/GCK-like kinase are provided. Effectiveness of antisense oligonucleotides was assayed by measuring kinase mRNA levels in cell cultures using real time PCR.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:467814 CAPLUS

DOCUMENT NUMBER: 135:225811

TITLE: Activation of p38, ERK1/2 and NIK Pathways is Required for IL-1 β and TNF- α -induced Chemokine Expression in Human Retinal Pigment Epithelial Cells

AUTHOR(S): Bian, Zong-Mei; Elner, Susan G.; Yoshida, Ayako; Kunkel, Steven L.; Su, Jia; Elner, Victor M.

CORPORATE SOURCE: Department of Ophthalmology, University of Michigan, Ann Arbor, MI, USA

SOURCE: Experimental Eye Research (2001), 73(1), 111-121

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chemokine secretion by human retinal pigment epithelium (hRPE) in response to IL-1 β and TNF- α occurs in infectious and noninfectious retinal diseases. In this study, the roles of p38 kinase and extracellular signal-regulated kinase (ERK) signaling pathways were investigated for IL-1 β - or TNF- α -induced IL-8 and MCP-1 secretion by hRPE cells. Treatment of hRPE cells with IL-1 β or TNF- α caused increased steady-state IL-8 and MCP-1 mRNA levels and protein secretion. Stimulation of hRPE with IL-1 β and TNF- α resulted in degradation of I κ B- α , nuclear translocation of NF- κ B, and prominent increases in p38 and ERK1/2 phosphorylation for as little as 3 min. The induced IL-8 and MCP-1 mRNA and proteins were partially suppressed by U0126, a specific MEK inhibitor, and by SB202190, a selective p38 inhibitor. This induction was completely blocked by simultaneous administration of the two drugs or by incubation with inhibitors for activation of NF- κ B such as BAY11-7085, CAPE, and parthenolide. These results suggest that co-activation of MEK/ERK and p38 pathways as well as activation of NIK pathway are essential for IL-1 β - and TNF- α -stimulation of IL-8 and MCP-1 gene expression in hRPE cells. Furthermore, co-administration of U0126 and SB202190 did not affect the induced degradation of I κ B- α and NF- κ B nuclear translocation, indicating that NF- κ B is activated by IL-1 β and TNF- α independently of activation of MEK/MAPK and p38 pathways in hRPE cells. (c) 2001 Academic Press.

REFERENCE COUNT: 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:566073 CAPLUS

DOCUMENT NUMBER: 131:198629

TITLE: A novel inhibitor of the inflammatory response induced by TNF α and IL-1

INVENTOR(S): Greene, Warner C.; Lin, Xin; Gelezuinas, Romas

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943704	A1	19990902	WO 1999-US4110	19990225 <--
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9928778	A	19990915	AU 1999-28778	19990225 <--
US 6265538	B1	20010724	US 1999-257703	19990225 <--
US 20020042499	A1	20020411	US 2001-871889	20010601 <--

US 6645728 B2 20031111

PRIORITY APPLN. INFO.: US 1998-76299P P 19980227
 US 1999-257703 A3 19990225
 WO 1999-US4110 W 19990225

AB The present invention provides the mol. basis for cytokine induction of NF- κ B-dependent immune and inflammatory responses, emphasizing a role for both NIK-NIK (NIK is NF- κ B-inducing kinase) and NIK-IKK (IKK is I κ B-specific kinase) protein-protein interactions. A relatively small region of NIK selectively impairs the NIK-IKK interaction. The present invention provides a novel and highly specific method for modulating NF- κ B-dependent immune, inflammatory, and anti-apoptotic responses, based on interruption of the critical protein-protein interaction of NIK and IKK. The present invention provides methods for inhibiting NF- κ B-dependent gene expression, using mutant NIK proteins. One embodiment of the present invention provides kinase-deficient NIK mutant proteins that inhibit activation of IKK. Another embodiment of the invention provides N-terminus NIK mutant proteins that bind IKK, thus inhibiting NIK/IKK interaction.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:407771 CAPLUS
 DOCUMENT NUMBER: 131:153360
 TITLE: Therapeutic Potential and Strategies for Inhibiting Tumor Necrosis Factor- α
 AUTHOR(S): Newton, Robert C.; Decicco, Carl P.
 CORPORATE SOURCE: Departments of Inflammatory Diseases Research and Chemical and Physical Sciences, Exp. Station, The DuPont Pharmaceuticals Company, Wilmington, DE, 19880-0500, USA

SOURCE: Journal of Medicinal Chemistry (1999), 42(13), 2295-2314
 CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with 249 refs. on tumor necrosis factor- α (TNF) as a validated target for drug discovery. The authors objective is to move beyond compds. that are currently under study and, using data generated from both mechanistic and compound discovery research, identify sites amenable to the design of small-mol. therapeutics. Some of the targets discussed are NF- κ B, the kinases NIK or IKK, mechanisms that link surface receptors to NIK, the regulation of TNF expression by cAMP modulation or MAP kinase inhibition, phosphodiesterases or p38 inhibition, gene regulation at the transcriptional level, any of the aspects of the TNF receptor-signaling complex (especially TRAF-2 or PEG3) or the regulation of TNF-induced gene expression by MAP kinase inhibition.

REFERENCE COUNT: 249 THERE ARE 249 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 45 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004388694 EMBASE
 TITLE: Tendon healing in vitro: Activation of NIK, IKK α , IKK β , and NF- κ B genes in signal pathway and proliferation of tenocytes.
 AUTHOR: Tang, Jin Bo, Dr. (correspondence); Xu, Yan; Wang, Xiao Tian

CORPORATE SOURCE: jbtang@rics.bwh.harvard.edu
 AUTHOR: Tang, Jin Bo, Dr. (correspondence); Xu, Yan; Wang, Xiao
 Tian
 CORPORATE SOURCE: Hand Surgery Research Center, Department of Hand Surgery,
 Affil. Hosp. of Nantong Med. College. jbtang@rics.bwh.harva
 rd.edu
 AUTHOR: Tang, Jin Bo, Dr. (correspondence)
 CORPORATE SOURCE: Gene Therapy and Tissue Engineering, Surgical Research-133
 North Campus, Roger Williams Medical Center, 825 Chalkstone
 Avenue, Providence, RI 02908-4735, United States.
 jbtang@rics.bwh.harvard.edu
 SOURCE: Plastic and Reconstructive Surgery, (May 2004)
 Vol. 113, No. 6, pp. 1703-1711.
 Refs: 35
 ISSN: 0032-1052 CODEN: PRSUAS
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 021 Developmental Biology and Teratology
 022 Human Genetics
 029 Clinical and Experimental Biochemistry
 009 Surgery
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 30 Sep 2004
 Last Updated on STN: 30 Sep 2004

AB Initiation of DNA transcription and proliferation of tendon cells are critical to tendon healing and require pivotal signals to the nucleus. Exploring intracellular signaling pathways pertinent to the healing process may reveal new approaches to accelerating the healing rate of the tendon. The authors investigated expression of NIK, IKK α , IKK β , and NF- κ B genes in the signal pathway and tenocyte proliferation in an in vitro model in which cultured tenocytes were exposed to basic fibroblast growth factor (bFGF). Tenocytes were obtained from explant culture of rabbit intrasynovial tendons and were treated with bFGF at concentrations of 0, 2, or 10 ng/ml. Levels of expression of a series of genes for key factors along the signaling route-nuclear factor (NF)- κ B-inducing kinase, inhibitor of κ B kinase alpha and beta, and the NF- κ B-were examined by quantitative analysis of products of reverse transcription and multiplex polymerase chain reactions. Proliferation of the cells was assessed with evaluation of growth curves and immunochemical labeling of the DNA of the cells. Expression levels of NIK, IKK α , IKK β , and NF- κ B genes were significantly increased by bFGF at concentrations of 2 and 10 ng/ml. Western blot confirmed the increase of NF- κ B in the tenocytes. The proliferation rate of the cells was significantly promoted by bFGF. Expression of these genes increased proportionately to the amounts of bFGF stimulating the cells and was correlated with increases in the proliferation rate. This study showed that expression of a series of genes along the NF- κ B pathway was remarkably promoted by bFGF. The effects were proportionate to in vitro cell proliferation rate. Results of the study suggest that activation of a series of genes along the NF- κ B pathway may play a pivotal role in initiating cell proliferation during the healing process of intrasynovial tendons. As activation of genes in signal transduction pathways is a new field in the biology of growth factor action with tremendous potential in promoting tissue repairs, manipulation of expression of a series of genes along the NF- κ B pathway can be a new target of enhancing tendon healing through molecular mechanisms.

L5 ANSWER 44 OF 45 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
 ACCESSION NUMBER: 2003304406 EMBASE

TITLE: Stretch-induced IL-8 depends on c-Jun NH(2)-terminal and nuclear factor- κ B-inducing kinases.

AUTHOR: Li, Li-Fu; Ouyang, Bin; Choukroun, Gabriel; Matyal, Robina; Mascarenhas, Marcella; Jafari, Behrouz; Bonventre, Joseph V.; Quinn, Deborah A. (correspondence)

CORPORATE SOURCE: Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, United States.

AUTHOR: Force, Thomas

CORPORATE SOURCE: Molec. Cardiology Research Institute, Department of Medicine, Tufts University School of Medicine, Boston, MA 02111, United States.

AUTHOR: Li, Li-Fu

CORPORATE SOURCE: Chang Gung University, Tao-Yuan 333, Taiwan, Province of China.

AUTHOR: Choukroun, Gabriel

CORPORATE SOURCE: Int. Med. and Nephrology Department, Amiens Hospital, 80054 Amiens, France.

AUTHOR: Quinn, Deborah A. (correspondence)

CORPORATE SOURCE: Mass. General Hospital, Pulmonary and Critical Care Unit, 55 Fruit St., Boston, MA 02114, United States.

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (1 Aug 2003) Vol. 285, No. 2 29-2, pp. L464-L475.

Refs: 45

ISSN: 1040-0605 CODEN: APLPE7

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
029 Clinical and Experimental Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Aug 2003
Last Updated on STN: 14 Aug 2003

AB Positive pressure ventilation with large tidal volumes has been shown to cause release of cytokines, including interleukin (IL)-8. The mechanisms regulating lung stretch-induced cytokine production are unclear. We hypothesized that stretch-induced IL-8 production is dependent on the activation of the mitogen-activated protein kinases, c-Jun NH(2)-terminal kinases (JNK), p38, and/or extracellular signal-regulated kinase (ERK) 1/2. We exposed A549 cells, a type II-like alveolar epithelial cell line, to cyclic stretch at 20 cycles/min for 5 min-2 h. Cyclic stretch induced IL-8 protein production, IL-8 mRNA expression, and JNK activation, but only transient activation of p38 and ERK1/2. Inhibition of stretch-induced JNK activation by adenovirus-mediated gene transfer of stress-activated protein kinase (SEK-1), a dominant-negative mutant of SEK-1, the immediate upstream activator of the JNKs, and pharmacological JNK inhibitor II SP-600125 blocked IL-8 mRNA expression and attenuated IL-8 production. Inhibition of p38 and ERK1/2 did not affect stretch-induced IL-8 production. Stretch-induced activation NF- κ B and activator protein (AP)-1 was blocked by NF- κ B inhibitor and JNK inhibitor, respectively. An NF-IL-6 site was not essential for cyclic stretch-induced IL-8 promoter activity. Stretch also induced NF- κ B-inducing kinase (NIK) activation, and inhibition of NF- κ B attenuated IL-8 mRNA expression and IL-8 production. We conclude that stretch-induced transcriptional regulation of IL-8 mRNA and IL-8 production was via activation of AP-1 and NF- κ B and was dependent on JNK and NIK activation, respectively.

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ACCESSION NUMBER: 2002225762 EMBASE
 TITLE: Differential requirement for NF- κ B-inducing kinase in the induction of NF- κ B by IL-1 β , TNF- α , and Fas.
 AUTHOR: Russo, Maria P.; Bennett, Brydon L.; Manning, Anthony M.; Brenner, David A.; Jobin, Christian (correspondence)
 CORPORATE SOURCE: Div. of Digestive Diseases, Glaxo Bldg., Univ. of North Carolina, Chapel Hill, Chapel Hill, NC 27599-7038, United States. Job@med.unc.edu
 SOURCE: American Journal of Physiology - Cell Physiology, (2002) Vol. 283, No. 1 52-1, pp. C347-C357.
 Refs: 65
 ISSN: 0363-6143 CODEN: AJPCDD
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 029 Clinical and Experimental Biochemistry
 005 General Pathology and Pathological Anatomy
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 11 Jul 2002
 Last Updated on STN: 11 Jul 2002
 AB In this study, we examined the role of the nuclear factor- κ B (NF- κ B)-inducing kinase (NIK) in distinct signaling pathways leading to NF- κ B activation. We show that a dominant-negative form of NIK (dnNIK) delivered by adenoviral (Ad5dnNIK) vector inhibits Fas-induced I κ B α phosphorylation and NF- κ B-dependent gene expression in HT-29 and HeLa cells. Interleukin (IL)-1 β - and tumor necrosis factor- α (TNF- α)-induced NF- κ B activation and κ B-dependent gene expression are inhibited in HeLa cells but not in Ad5dnNIK-infected HT-29 cells. Moreover, Ad5dnNIK failed to sensitize HT-29 cells to TNF- α -induced apoptosis at an early time point. However, cytokine- and Fas-induced signals to NF- κ B are finally integrated by the I κ B kinase (IKK) complex, since I κ B α phosphorylation, NF- κ B DNA binding activity, and IL-8 gene expression were strongly inhibited in HT-29 and HeLa cells overexpressing dominant-negative IKK β (Ad5dnIKK β). Our findings support the concept that cytokine signaling to NF- κ B is redundant at the level of NIK. In addition, this study demonstrates for the first time the critical role of NIK and IKK β in Fas-induced NF- κ B signaling cascade.

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enhanced
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Applications
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pre-registered REACH substances
NEWS 8 NOV 21 CAS patent coverage to include exemplified prophetic
substances identified in English-, French-, German-,
and Japanese-language basic patents from 2004-present
NEWS 9 NOV 26 MARPAT enhanced with FSORT command
NEWS 10 NOV 26 MEDLINE year-end processing temporarily halts
availability of new fully-indexed citations
NEWS 11 NOV 26 CHEMSAFE now available on STN Easy
NEWS 12 NOV 26 Two new SET commands increase convenience of STN
searching
NEWS 13 DEC 01 ChemPort single article sales feature unavailable
NEWS 14 DEC 12 GBFULL now offers single source for full-text
coverage of complete UK patent families
NEWS 15 DEC 17 Fifty-one pharmaceutical ingredients added to PS
NEWS 16 JAN 06 The retention policy for unread STNmail messages
will change in 2009 for STN-Columbus and STN-Tokyo

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

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specific topic.

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FILE 'HOME' ENTERED AT 15:51:25 ON 06 JAN 2009

=> D Hist

(FILE 'HOME' ENTERED AT 15:51:25 ON 06 JAN 2009)

=> File .Gerry2MBCE
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.22	0.22

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:51:58 ON 06 JAN 2009

FILE 'BIOSIS' ENTERED AT 15:51:58 ON 06 JAN 2009
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FILE 'CAPLUS' ENTERED AT 15:51:58 ON 06 JAN 2009
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```
=> S (NIK OR SIVA) (S) modulat? (S) (immune(6A)disorder) AND pd<=20041130
  1 FILES SEARCHED...
  3 FILES SEARCHED...
L1      0 (NIK OR SIVA) (S) MODULAT? (S) (IMMUNE(6A) DISORDER) AND PD<=200
      41130

=> S (NIK(S)SIVA) (S) complex (S) (immune? OR Leukemia) and pd<=20041130
  1 FILES SEARCHED...
L2      0 (NIK(S) SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=2004
      1130

=> S (NIK(S)SIVA) (S) complex (S) (immune? OR Leukemia) AND pd<=20041130
  1 FILES SEARCHED...
L3      0 (NIK(S) SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=2004
      1130

=> S (NIK(S)SIVA) (S) complex AND pd<=20041130
  1 FILES SEARCHED...
L4      0 (NIK(S) SIVA) (S) COMPLEX AND PD<=20041130

=> S (NIK(S)SIVA) (S) Binding AND pd<=20041130
  1 FILES SEARCHED...
L5      0 (NIK(S) SIVA) (S) BINDING AND PD<=20041130

=> S (NIK (S) SIVA) (S) Binding AND pd<=20041130
  1 FILES SEARCHED...
L6      0 (NIK (S) SIVA) (S) BINDING AND PD<=20041130

=> S (NIK(S)SIVA) (S) Binding
L7      1 (NIK(S) SIVA) (S) BINDING

=> D ibib abs
```

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:490302 CAPLUS
DOCUMENT NUMBER: 143:42678
TITLE: Antibodies specific to SIVA proteins for identifying
immune modulators to treat immune diseases
WALLACH, David; Ramakrishnan, Parameswaran; Wang,
Wangxia; Shmushkovich, Taisia
INVENTOR(S): Yeda Research and Development Ltd., Israel
PATENT ASSIGNEE(S):
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051423	A2	20050609	WO 2004-IL1095	20041130
WO 2005051423	A3	20051215		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
 SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

AU 2004292872	A1	20050609	AU 2004-292872	20041130
CA 2547459	A1	20050609	CA 2004-2547459	20041130
EP 1689786	A2	20060816	EP 2004-799393	20041130

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
 HR, IS, YU

JP 2007517501	T	20070705	JP 2006-540777	20041130
NO 2006003037	A	20060821	NO 2006-3037	20060629
US 20080025968	A1	20080131	US 2007-580542	20070302

IL 2003-159133 A 20031130
 IL 2004-163250 A 20040728
 WO 2004-IL1095 W 20041130

PRIORITY APPLN. INFO.:

AB Methods and agents for immune modulation and methods for identifying
 immune modulators are provided. The methods comprise use of antibodies
 that target NIK and NIK-binding proteins
 (e.g. SIVA, SIVAL and SIVA2 proteins) participating in both
 canonical and alternative NF- κ B activation pathway. The agent may
 also be a small interfering RNA mol. or ribozyme. The immune diseases,
 involving abnormal function or level of Blys/BAFF, CD27, SIVA and/or NIK,
 include multiple myeloma, AIDS, Sjogren's syndrome, B cell chronic
 lymphocytic leukemia, systemic lupus erythematosus, inflammatory colon
 disease, systemic inflammatory response syndrome, multiple organ
 disinfection syndrome, and acute respiratory distress syndrome.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> S (NIK (S) SIVA) (S) interaction AND pd<=20041130
 1 FILES SEARCHED...
 L8 0 (NIK (S) SIVA) (S) INTERACTION AND PD<=20041130

=> S (NIK OR SIVA) (S) treatment (S) leukemia AND pd<=20041130
 1 FILES SEARCHED...
 L9 0 (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA AND PD<=20041130

=> S (NIK OR SIVA) (S) treatment (S) leukemia
 L10 0 (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA

=> S (NIK OR SIVA) (S) treatment
 L11 157 (NIK OR SIVA) (S) TREATMENT

=> S S (NIK OR SIVA) (S) treatment (P) (immune disorder) AND pd<=20041130
 MISSING OPERATOR 'S (NIK'
 The search profile that was entered contains terms or
 nested terms that are not separated by a logical operator.

=> S (NIK OR SIVA) (S) treatment (P) (immune disorder) AND pd<=20041130
 1 FILES SEARCHED...
 L12 0 (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER) AND PD<=200411
 30

=> S (NIK OR SIVA) (S) treatment (P) (immune disorder)

L13 0 (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER)

=> Dup rem L11

PROCESSING COMPLETED FOR L11

L14 76 DUP REM L11 (81 DUPLICATES REMOVED)

ANSWERS '1-32' FROM FILE MEDLINE

ANSWERS '33-38' FROM FILE BIOSIS

ANSWERS '39-73' FROM FILE CAPLUS

ANSWERS '74-76' FROM FILE EMBASE

=> D TI L14 1-76

L14 ANSWER 1 OF 76 MEDLINE on STN DUPLICATE 1
TI Antimetastatic effect of a small-molecule vacuolar H⁺-ATPase inhibitor in
in vitro and in vivo preclinical studies.

L14 ANSWER 2 OF 76 MEDLINE on STN DUPLICATE 2
TI NF-kappaB-inducing kinase regulates cyclooxygenase 2 gene expression in
macrophages by phosphorylation of PU.1.

L14 ANSWER 3 OF 76 MEDLINE on STN DUPLICATE 3
TI Interferon-gamma sensitizes hepatitis B virus-expressing hepatocarcinoma
cells to 5-fluorouracil through inhibition of hepatitis B virus-mediated
nuclear factor-kappaB activation.

L14 ANSWER 4 OF 76 MEDLINE on STN DUPLICATE 6
TI Down-regulation of iNOS and TNF-alpha expression by kaempferol via
NF-kappaB inactivation in aged rat gingival tissues.

L14 ANSWER 5 OF 76 MEDLINE on STN DUPLICATE 7
TI NIK is involved in nucleosomal regulation by enhancing histone H3
phosphorylation by IKKalpha.

L14 ANSWER 6 OF 76 MEDLINE on STN DUPLICATE 8
TI An RNA interference-based screen identifies MAP4K4/NIK as a negative
regulator of PPARGamma, adipogenesis, and insulin-responsive hexose
transport.

L14 ANSWER 7 OF 76 MEDLINE on STN DUPLICATE 9
TI Interleukin-1beta induction of NFkappaB is partially regulated by
H2O2-mediated activation of NFkappaB-inducing kinase.

L14 ANSWER 8 OF 76 MEDLINE on STN DUPLICATE 10
TI NIK-333 inhibits growth of human T-cell leukemia virus type I-infected
T-cell lines and adult T-cell leukemia cells in association with blockade
of nuclear factor-kappaB signal pathway.

L14 ANSWER 9 OF 76 MEDLINE on STN DUPLICATE 12
TI Efficacy of micafungin alone or in combination against experimental
pulmonary aspergillosis.

L14 ANSWER 10 OF 76 MEDLINE on STN DUPLICATE 13
TI Expression of Siva-1 protein or its putative amphipathic helical region
enhances cisplatin-induced apoptosis in breast cancer cells: effect of
elevated levels of BCL-2.

L14 ANSWER 11 OF 76 MEDLINE on STN DUPLICATE 14
TI Biological and chemical inhibitors of NF-kappaB sensitize SiHa cells to
cisplatin-induced apoptosis.

L14 ANSWER 12 OF 76 MEDLINE on STN DUPLICATE 15
TI The proapoptotic gene SIVA is a direct transcriptional target for the

tumor suppressors p53 and E2F1.

- L14 ANSWER 13 OF 76 MEDLINE on STN DUPLICATE 16
TI NF-kappaB activation by the chemopreventive dithiolethione oltipraz is exerted through stimulation of MEKK3 signaling.
- L14 ANSWER 14 OF 76 MEDLINE on STN DUPLICATE 17
TI Role of reactive oxygen species, glutathione and NF-kappaB in apoptosis induced by 3,4-methylenedioxymethamphetamine ("Ecstasy") on hepatic stellate cells.
- L14 ANSWER 15 OF 76 MEDLINE on STN DUPLICATE 18
TI The transcriptional activity of the APP intracellular domain-Fe65 complex is inhibited by activation of the NF-kappaB pathway.
- L14 ANSWER 16 OF 76 MEDLINE on STN DUPLICATE 19
TI Prevalence of asthma and related symptoms in Sivas, Central Anatolia.
- L14 ANSWER 17 OF 76 MEDLINE on STN DUPLICATE 20
TI Regulation of Fas-mediated apoptosis by NF-kappaB activity in human hepatocyte derived cell lines.
- L14 ANSWER 18 OF 76 MEDLINE on STN DUPLICATE 21
TI 5-Fluorouracil suppression of NF-KappaB is mediated by the inhibition of Ikappab kinase activity in human salivary gland cancer cells.
- L14 ANSWER 19 OF 76 MEDLINE on STN DUPLICATE 22
TI Thioredoxin inhibits tumor necrosis factor- or interleukin-1-induced NF-kappaB activation at a level upstream of NF-kappaB-inducing kinase.
- L14 ANSWER 20 OF 76 MEDLINE on STN DUPLICATE 23
TI Nuclear factor kappa B: a pivotal role in the systemic inflammatory response syndrome and new target for therapy.
- L14 ANSWER 21 OF 76 MEDLINE on STN DUPLICATE 24
TI NIK-247 induces long-term potentiation of synaptic transmission in the CA1 region of rat hippocampal slices through M2 muscarinic receptors.
- L14 ANSWER 22 OF 76 MEDLINE on STN DUPLICATE 25
TI Effects of NIK-247 on cholinesterase and scopolamine-induced amnesia.
- L14 ANSWER 23 OF 76 MEDLINE on STN DUPLICATE 26
TI Synthesis of estimated metabolites of 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinoline monohydrochloride monohydrate (NIK-247). II. Synthesis of dihydroxylated metabolites.
- L14 ANSWER 24 OF 76 MEDLINE on STN DUPLICATE 27
TI Synthesis of estimated metabolites of 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta[b]quinoline monohydrochloride monohydrate (NIK-247). I. Synthesis of mono-hydroxylated metabolites.
- L14 ANSWER 25 OF 76 MEDLINE on STN DUPLICATE 28
TI Role of adrenergic neuronal activity in the yawning induced by tacrine and NIK-247 in rats.
- L14 ANSWER 26 OF 76 MEDLINE on STN DUPLICATE 29
TI Effect of 9-amino-2,3,5,6,7,8-hexahydro-1H-cyclopenta-(b)-quinoline monohydrate hydrochloride (NIK-247) on cholinergic enzyme activity in rats.
- L14 ANSWER 27 OF 76 MEDLINE on STN DUPLICATE 30
TI Effects of the novel compound NIK-247 on impairment of passive avoidance

response in mice.

- L14 ANSWER 28 OF 76 MEDLINE on STN
TI [Determination of tick species and treatment of cows, sheep and goats in the Sivas-Zara region].
Sivas-Zara yoresindeki sigir, koyun ve kecelerde kene turlerinin belirlenmesi ve sagaltimi.
- L14 ANSWER 29 OF 76 MEDLINE on STN
TI [Treatment of atherosclerotic patients with radon-carbon dioxide baths at the Khmel'nik health resort].
Lechenie bol'nykh aterosklerozom radonovo-uglekislymi vannami kurorta Khmel'nik.
- L14 ANSWER 30 OF 76 MEDLINE on STN
TI [Treatment of patients with arteriosclerosis at the Khmel'nik health resort].
Lechenie bol'nykh aterosklerozom na kurorte Khmel'nik.
- L14 ANSWER 31 OF 76 MEDLINE on STN
TI [Treatment with radon-carbonate baths of the health resort Khmel'nik of the patients with endarteritis obliterans].
Lechenie radonovo-uglekislymi vannami kurorta khmel'nik bol'nykh obliterieuiushchim zndarteriitom.
- L14 ANSWER 32 OF 76 MEDLINE on STN
TI [Combined treatment of patients with stomach and duodenal ulcer with Kuial'nik No.4 mineral water].
Kompleсноe lechenie bol'nykh iazvennoi bolezni'iu zheludka i dvenadtsatiperstnoi kiskhki s ispol'zovaniem mineral'noi vody Kuial'nik Number 4.
- L14 ANSWER 33 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 4
TI Thiazolidinediones enhance skeletal muscle triacylglycerol synthesis while protecting against fatty acid-induced inflammation and insulin resistance.
- L14 ANSWER 34 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 5
TI Effects of water deficit and selenium on common buckwheat (*Fagopyrum esculentum* Moench.) plants.
- L14 ANSWER 35 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 11
TI Performance assessment of a wastewater treatment plant treating weak campus wastewater.
- L14 ANSWER 36 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 31
TI EFFECTS OF A NOVEL DRUG 8 AMINO-2 3 5 6 7
8-HEXAHYDRO-1H-CYCLOPENTA-B-QUINOLINE MONOHYDRATE HYDROCHLORIDE NIK-247 ON CENTRAL CHOLINERGIC SYSTEMS.
- L14 ANSWER 37 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
TI Induction of PTEN expression, mediated through the JNK/NFkappaB pathway, is associated with intestinal differentiation.
- L14 ANSWER 38 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
TI SIVA is upregulated in response to p53 mediated neuronal cell death.

L14 ANSWER 39 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Microorganisms as carriers of nucleotide sequences coding for antigens and protein toxins for use in disease treatment

L14 ANSWER 40 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI TRAF2?TRAF3/p53 biomarkers and assays for the treatment of cancer with a lymphotoxin- β receptor activating agent

L14 ANSWER 41 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Immunotherapy for clinically isolated syndrome? Not necessarily...

L14 ANSWER 42 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI The pro-apoptotic Siva-1 protein plays a significant role in DNA damage-induced programmed cell death

L14 ANSWER 43 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Diagnostic agents and uses therefor

L14 ANSWER 44 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI SIVA2 ubiquitination and/or degradation-related activity and modulators thereof

L14 ANSWER 45 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Potassium channel blockers for treatment of migraine and headache

L14 ANSWER 46 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Characterization and chemical treatment of a medium-large scale mixed-organized industrial estate (OIE)

L14 ANSWER 47 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Gene expression markers for the identification, assessment, and treatment, and responsiveness of cancer using proteasome inhibition or glucocorticoid therapy

L14 ANSWER 48 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Honokiol derivatives for the treatment of proliferative disorders

L14 ANSWER 49 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Genetic alterations useful for the response prediction of malignant neoplasia to taxane-based medical treatments

L14 ANSWER 50 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Preparation of leukocytes and treatment of defects of cellular immunity with leukocyte homogenates having a molecular weight of less than 10,000 dalton

L14 ANSWER 51 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Molluscum contagiosum virus MC160 protein compositions for treatment of inflammation

L14 ANSWER 52 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Pharmaceuticals agents comprising blood components 10 kDa and their use for prophylaxis and treatment of defects of the immune system

L14 ANSWER 53 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Use of a modulator of gene expression in the treatment of cancer

L14 ANSWER 54 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Methods and compositions for the treatment of cancer with oligonucleotides directed against Egr-1

L14 ANSWER 55 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

TI Therapeutic and carrier molecules

L14 ANSWER 56 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Methods using a combination of a p38 MAP kinase inhibitor with another active agent for the treatment of chronic obstructive pulmonary disease (COPD) and pulmonary hypertension

L14 ANSWER 57 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Pyrazoloisoquinoline derivatives as kinase inhibitors, and their preparation, pharmaceutical compositions, and use in the treatment of diseases involving increased NIK activity.

L14 ANSWER 58 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Gene expression profiles and methods for prognosis and treatment of solid tumors

L14 ANSWER 59 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Methods for the identification, assessment, and treatment of patients with proteasome inhibition therapy

L14 ANSWER 60 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI New members of the germinal center kinase family identified by sequence homology and their diagnostic and therapeutic uses

L14 ANSWER 61 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Preparation of pyrazoloisoquinolines as NF- κ B-inducing kinase (NIK) inhibitors

L14 ANSWER 62 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Modulation of NIK with IL-2 common γ chain and therapeutic uses thereof

L14 ANSWER 63 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Modulating interaction of IL-2 with NIK by derivatives of the IL-2 common gamma chain, and therapeutic uses thereof

L14 ANSWER 64 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Characteristics and treatability of hospital (medical) wastewaters

L14 ANSWER 65 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Diagnostic and drug screening use of cellular kinases involved in human cytomegalovirus infection and treatment of HCMV infection using kinase inhibitors

L14 ANSWER 66 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Gene expression profiling by cDNA array in human hepatoma cell line in response to cisplatin treatment

L14 ANSWER 67 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Activators for peroxisome proliferator-activated receptor containing polyprenyl compounds

L14 ANSWER 68 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Ipidacrine hydrochloride for treatment of Alzheimer's disease

L14 ANSWER 69 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Ipidacrine (NIK-247), a novel antidementia drug, rapidly enters the brain and improves scopolamine-induced amnesia in rats during the Morris water task

L14 ANSWER 70 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 TI I κ B kinase- β : NF- κ B activation and complex formation with

I κ B kinase- α and NIK

- L14 ANSWER 71 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
TI Effects of NIK-247 on carbon monoxide-induced impairment of passive avoidance in mice
- L14 ANSWER 72 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
TI Effect of some mutagenic factors on the resistance of spring wheat to yellow rust
- L14 ANSWER 73 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
TI Preliminary treatment of synthetic rubber
- L14 ANSWER 74 OF 76 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
TI Thiazolidinediones enhance skeletal muscle triacylglycerol synthesis while protecting against fatty acid-induced inflammation and insulin resistance.
- L14 ANSWER 75 OF 76 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
TI The effects of claritromycin added to atorvastatin treatment on serum lipid profiles: A randomised clinical trial.
- L14 ANSWER 76 OF 76 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
TI Solution and resource-oriented addiction treatment with the choices of abstinence or controlled drinking.

=> Log off H

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 16:17:08 ON 06 JAN 2009

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 16:48:05 ON 06 JAN 2009
FILE 'MEDLINE' ENTERED AT 16:48:05 ON 06 JAN 2009
FILE 'BIOSIS' ENTERED AT 16:48:05 ON 06 JAN 2009
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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	182.86	183.08
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.82	-0.82

=> D hist

(FILE 'HOME' ENTERED AT 15:51:25 ON 06 JAN 2009)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:51:58 ON 06 JAN 2009

L1 0 S (NIK OR SIVA) (S) MODULAT? (S) (IMMUNE(6A)DISORDER) AND PD<=2
L2 0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L3 0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L4 0 S (NIK(S)SIVA) (S) COMPLEX AND PD<=20041130
L5 0 S (NIK(S)SIVA) (S) BINDING AND PD<=20041130
L6 0 S (NIK (S) SIVA) (S) BINDING AND PD<=20041130
L7 1 S (NIK(S)SIVA) (S) BINDING
L8 0 S (NIK (S) SIVA) (S) INTERACTION AND PD<=20041130
L9 0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA AND PD<=20041130
L10 0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA
L11 157 S (NIK OR SIVA) (S) TREATMENT
L12 0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER) AND PD<=200
L13 0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER)
L14 76 DUP REM L11 (81 DUPLICATES REMOVED)

=> D Ibib abs 2,4,6,10,11,13,20,38,40,41,43,52,53,55,57,58,61,70

L14 ANSWER 2 OF 76 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2007689411 MEDLINE
DOCUMENT NUMBER: PubMed ID: 18025233
TITLE: NF-kappaB-inducing kinase regulates cyclooxygenase 2 gene expression in macrophages by phosphorylation of PU.1.
AUTHOR: Azim Anser C; Wang Xuerong; Park Gye Young; Sadikot Ruxana T; Cao Hongmei; Mathew Bijji; Atchison Michael; van Breenen Richard B; Joo Myungsoo; Christman John W
CORPORATE SOURCE: Department of Medicine, University of Illinois, Chicago, IL 60612, USA.
CONTRACT NUMBER: HL075557 (United States NHLBI)
HL66196 (United States NHLBI)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2007 Dec 1) Vol. 179, No. 11, pp. 7868-75.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200802
ENTRY DATE: Entered STN: 21 Nov 2007
Last Updated on STN: 6 Feb 2008
Entered Medline: 5 Feb 2008

AB Selective expression of cyclooxygenase 2 (COX-2) by macrophages could have an important role in the pathobiology of inflammation. We reported a functional synergism between PU.1 and other transcription factors that contributes to COX-2 gene expression in macrophages. PU.1 resides in the nuclear compartment and is activated by phosphorylation to bind to cognate DNA elements containing a 5'-GGAA/T-3' motif, but the involved kinase has not been discovered. We tested the hypothesis that NF-kappaB-inducing kinase (NIK) regulates COX-2 gene expression in macrophages through inducible phosphorylation of PU.1. Our initial experiments showed an in vitro protein-protein binding interaction between myc-NIK and GST-PU.1. Purified myc-NIK had a strong in vitro kinase activity for purified GST-PU.1, and this activity and production of COX-2 protein is blocked by treatment with a nonspecific kinase inhibitor, 5,6-dichloro-1-beta-D-ribofuranosylbenzimidazole. We used short interfering RNA to develop a stable NIK knockdown macrophage

cell line that had an approximately 50% decrease in COX-2 protein production and decreased generation of PGD(2), and this was correlated with decreased binding of activated PU.1 to the COX-2 promoter in response to treatment with endotoxin. These findings suggest a novel role for NIK in mediating COX-2 gene expression in endotoxin-treated macrophages by a mechanism that involves phosphorylation of PU.1.

L14 ANSWER 4 OF 76 MEDLINE on STN DUPLICATE 6
 ACCESSION NUMBER: 2007390714 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 17278014
 TITLE: Down-regulation of iNOS and TNF-alpha expression by kaempferol via NF-kappaB inactivation in aged rat gingival tissues.
 AUTHOR: Kim Hyung Keun; Park Hae Ryoung; Lee Jun Sik; Chung Tae Sung; Chung Hae Young; Chung Jin
 CORPORATE SOURCE: Department of Oral Pathology, School of Dentistry, Pusan National University, Busan, 602-739, Korea.
 SOURCE: Biogerontology, (2007 Aug) Vol. 8, No. 4, pp. 399-408. Electronic Publication: 2007-02-03. Journal code: 100930043. ISSN: 1389-5729.
 PUB. COUNTRY: Netherlands
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200709
 ENTRY DATE: Entered STN: 6 Jul 2007
 Last Updated on STN: 22 Sep 2007
 Entered Medline: 21 Sep 2007

AB The primary objective of this study was to evaluate the ability and mechanism of action of kaempferol, which is contained in extracts from Nelumbo nucifera, a well-known Oriental herb used in traditional medicine, with regard to the inhibition of iNOS and TNF-alpha expression in aged rat gingival tissues. We conducted an investigation into the age-related effects of kaempferol on reactive oxygen species (ROS) and GSH oxidative status in samples of aged gingival tissues. Western blotting was conducted in order to determine the expression of iNOS, TNF-alpha, p38 MAPK, NIK/IKK, p65 and IkappaBalpha in the sample tissues. Electrophoretic mobility shift assays (EMSA) were conducted in an effort to characterize the binding activities of NF-kappaB transcription factors in the aged rat gingival nuclear extracts. Our results indicate that kaempferol reduced ROS levels and augmented GSH levels in a dose-dependent manner in the aged gingival tissues. Kaempferol was shown to effect a significant reduction in iNOS and TNF-alpha protein levels, as compared to control gingival tissue samples. The results of Western blot analysis revealed that kaempferol treatment effected the reduction of iNOS and TNF-alpha expression, decreased nuclear p65 and increased cytosolic p65, down-regulation of Erk, p38, JNK and NIK/IKK expression. The EMSA results also indicated that kaempferol, when administered to the rat tissues, attenuated the NF-kappaB nuclear binding activity. Kaempferol may inhibit ROS generation via the inhibition of iNOS and TNF-alpha expression in aged gingival tissues, via the modulation of the NF-kappaB and mitogen-activated protein kinase (MAPK) pathways.

L14 ANSWER 6 OF 76 MEDLINE on STN DUPLICATE 8
 ACCESSION NUMBER: 2006093000 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 16461467
 TITLE: An RNA interference-based screen identifies MAP4K4/NIK as a negative regulator of PPARgamma, adipogenesis, and insulin-responsive hexose transport.
 AUTHOR: Tang Xiaqing; Guilherme Adilson; Chakladar Abhijit; Powelka Aimee M; Konda Silvana; Virbasius Joseph V;

CORPORATE SOURCE: Nicoloro Sarah M C; Straubhaar Juerg; Czech Michael P
 Program in Molecular Medicine, University of Massachusetts
 Medical School, Worcester, MA 01605, USA.
 CONTRACT NUMBER: DK30898 (United States NIDDK)
 SOURCE: DK60837-03 (United States NIDDK)
 Proceedings of the National Academy of Sciences of the
 United States of America, (2006 Feb 14) Vol. 103, No. 7,
 pp. 2087-92. Electronic Publication: 2006-02-03.
 Journal code: 7505876. ISSN: 0027-8424.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200604
 ENTRY DATE: Entered STN: 16 Feb 2006
 Last Updated on STN: 8 Apr 2006
 Entered Medline: 7 Apr 2006

AB The insulin-regulated glucose transporter GLUT4 is a key modulator of whole body glucose homeostasis, and its selective loss in adipose tissue or skeletal muscle causes insulin resistance and diabetes. Here we report an RNA interference-based screen of protein kinases expressed in adipocytes and identify four negative regulators of insulin-responsive glucose transport: the protein kinases PCTAIRE-1 (PCTK1), PFTAIRE-1 (PFTK1), IkappaB kinase alpha, and MAP4K4/NIK. Integrin-linked protein kinase was identified as a positive regulator of this process. We characterized one of these hits, MAP4K4/NIK, and found that it is unique among mitogen-activated protein (MAP) kinases expressed in cultured adipocytes in attenuating hexose transport. Remarkably, MAP4K4/NIK suppresses expression of the adipogenic transcription factors C/EBPalpha, C/EBPbeta, and PPARGgamma and of GLUT4 itself in these cells. RNA interference-mediated depletion of MAP4K4/NIK early in differentiation enhances adipogenesis and triglyceride deposition, and even in fully differentiated adipocytes its loss up-regulates GLUT4. Conversely, conditions that inhibit adipogenesis such as TNF-alpha treatment or depletion of PPARGgamma markedly up-regulate MAP4K4/NIK expression in cultured adipocytes. Furthermore, TNF-alpha signaling to down-regulate GLUT4 is impaired in the absence of MAP4K4/NIK, indicating that MAP4K4 expression is required for optimal TNF-alpha action. These results reveal a MAP4K4/NIK-dependent signaling pathway that potentially inhibits PPARGgamma-responsive gene expression, adipogenesis, and insulin-stimulated glucose transport.

L14 ANSWER 10 OF 76 MEDLINE on STN DUPLICATE 13
 ACCESSION NUMBER: 2005310826 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15958577
 TITLE: Expression of Siva-1 protein or its putative amphipathic helical region enhances cisplatin-induced apoptosis in breast cancer cells: effect of elevated levels of BCL-2.
 AUTHOR: Chu Fei; Barkinge John; Hawkins Sarah; Gudi Radhika; Salgia Ravi; Kanteti Prasad V S
 CORPORATE SOURCE: Department of Microbiology and Immunology, University of Illinois at Chicago, 60612, USA.
 CONTRACT NUMBER: GM56706 (United States NIGMS)
 SOURCE: Cancer research, (2005 Jun 15) Vol. 65, No. 12, pp. 5301-9.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 17 Jun 2005
Last Updated on STN: 9 Aug 2005
Entered Medline: 8 Aug 2005

AB cis-Diaminedichloroplatinum (II) (cisplatin) is routinely used to treat various types of cancers; however, a significant number develop resistance. One of the underlying factors that contribute to cisplatin resistance is the elevated level of BCL-2 and/or BCL-XL, which promotes cell survival. A potential method of overcoming such resistance is to use a potentiator that is capable of neutralizing the antiapoptotic effects of BCL-2/BCL-XL, such as Siva-1. We previously cloned the proapoptotic protein Siva-1 and showed a possible role for it in both extrinsic and intrinsic apoptosis. Using an adenovirus-based expression system, we now show that Siva-1 can synergize with cisplatin in inducing apoptosis in MCF7 and MDA-MB-231 breast cancer cells. In an anchorage-independent clonogenicity assay, MCF7/caspase-3 cells stably expressing Siva-1, but not the control cells, showed a dramatic decrease in the number of colonies formed on one-time cisplatin treatment. Further, we show that the unique putative amphipathic helical region (SAH) in Siva-1 (amino acid residues 36-55) is necessary and sufficient for the observed enhancement in cisplatin-induced apoptosis by Siva-1. Although cisplatin treatment results in significant elevation in the expression of Fas ligand and intracellular p21 levels, expression of Siva-1 has no additional benefit. Instead, the enhancement in apoptosis seems to be due to activation of intrinsic pathway that involves caspase-9 activation. Moreover, Siva-1 augments cisplatin-mediated cell death in MCF7 cells stably expressing BCL-2. We therefore propose that Siva-1 or its SAH region can be used as a potentiator of cisplatin-based chemotherapy.

L14 ANSWER 11 OF 76 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2005396712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16044419
TITLE: Biological and chemical inhibitors of NF-kappaB sensitize SiHa cells to cisplatin-induced apoptosis.
AUTHOR: Venkatraman Manickam; Anto Ruby John; Nair Asha; Varghese Merina; Karunakaran Devarajan
CORPORATE SOURCE: Division of Cancer Biology, Rajiv Gandhi Center for Biotechnology, Thiruvananthapuram, Kerala, India.
SOURCE: Molecular carcinogenesis, (2005 Sep) Vol. 44, No. 1, pp. 51-9.
Journal code: 8811105. ISSN: 0899-1987.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 2 Aug 2005
Last Updated on STN: 24 Sep 2005
Entered Medline: 23 Sep 2005

AB Cisplatin, a chemotherapeutic agent, is known to induce apoptosis of cancer cells. We examined the role of NF-kappaB during cisplatin-induced apoptosis in two human cervical cancer cell lines, HeLa and SiHa, known to differ in their response to cisplatin treatment. We found that SiHa cells were relatively more resistant than HeLa cells to the cytotoxic effects induced by cisplatin as measured by MTT assays. HeLa cells were more sensitive to the apoptotic effects induced by cisplatin as shown by increases in annexin staining, DNA fragmentation, and loss of mitochondrial membrane potential. Similarly the activities of caspases 3,

8, and 9 and cleavage of PARP induced by cisplatin were more in HeLa than SiHa cells. Cisplatin induced NF-kappaB DNA binding activity in HeLa and SiHa cells but not in primary cervical cells and the active DNA binding complex in SiHa cells consists of p50 and RelA heterodimers. However, when NF-kappaB DNA binding activity was blocked by chemical (curcumin, PDTc, or salicylic acid) or biological inhibitors (NIK-KM or IKK-beta DN), the cell viability was less in SiHa cells with cisplatin treatment, but these effects were not observed in HeLa cells. Similarly upon treatment with cisplatin SiHa cells had more activation of caspases compared to that seen in HeLa cells under conditions of NF-kappaB inhibition by biological or chemical inhibitors. These results suggest that NF-kappaB may contribute to the resistance of human cervical cancer cells to cisplatin and highlight the potential use of combination therapy involving cisplatin and NF-kappaB inhibitors.
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L14 ANSWER 13 OF 76 MEDLINE on STN DUPLICATE 16
 ACCESSION NUMBER: 2004312263 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 15047705
 TITLE: NF-kappaB activation by the chemopreventive dithiolethione oltipraz is exerted through stimulation of MEKK3 signaling.
 AUTHOR: Nho Chu Won; O'Dwyer Peter J
 CORPORATE SOURCE: Division of Hematology-Oncology, School of Medicine and Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.
 CONTRACT NUMBER: CA-78272 (United States NCI)
 SOURCE: The Journal of biological chemistry, (2004 Jun 18) Vol. 279, No. 25, pp. 26019-27. Electronic Publication: 2004-03-26.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200407
 ENTRY DATE: Entered STN: 25 Jun 2004
 Last Updated on STN: 25 Jul 2004
 Entered Medline: 23 Jul 2004

AB Chemoprevention by the dithiolethione analogue oltipraz (4-methyl-5-(2-pyrazinyl)-1,2-dithiole-3-thione) may occur through several mechanisms, among them stimulation of detoxication activity. The phase II detoxication enzyme, NAD(P)H:quinone oxidoreductase 1 (NQO1; EC 1.6.99.2) also known as quinone reductase (QR) is well established to undergo transcriptional activation following oltipraz treatment of colon cancer cells in culture. Promoter analysis of the QR gene in oltipraz-treated cells reveals the involvement of both the AP-1 and NF-kappaB elements in the response. The emerging role of NF-kappaB in cell survival prompted a fuller analysis of effects of oltipraz on this pathway. Oltipraz treatment of both HCT116 and HT29 cells results in the induction of proteins involved in both pathways of NF-kappaB activation, including p65, IkappaB kinase alpha (IKKalpha), IkappaB kinase beta (IKKbeta), and NF-kappaB-inducing kinase (NIK). IkappaBalpha total protein levels were unchanged, but phosphorylation of the inhibitor was also induced in both lines. Electrophoretic mobility shift assay (EMSA) analysis confirmed induction of protein binding to a consensus NF-kappaB element, and transcriptional activation was further confirmed using a reporter construct. Transcriptional activation of QR was decreased in a dose-dependent manner by dominant-negative NF-kappaB in both cell lines. The molecular mechanism that triggers IKK activation in response to oltipraz was also examined using inhibitory constructs of NIK and mitogen-activated protein kinase/extracellular signal-regulated kinase

kinase kinase 3 (MEKK3). We found that both MEKK3 and NIK exert effects on IKKalpha/beta activation, but through different pathways. Furthermore, the receptor-interacting protein (RIP) was found to interact strongly with MEKK3 during oltipraz-induced NF-kappaB signaling, implying a role for tumor necrosis factor receptor signaling in the action of oltipraz. These results implicate a novel signaling pathway for the action of oltipraz in QR gene regulation.

L14 ANSWER 20 OF 76 MEDLINE on STN DUPLICATE 23
 ACCESSION NUMBER: 1999092801 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9876974
 TITLE: Nuclear factor kappa B: a pivotal role in the systemic inflammatory response syndrome and new target for therapy.
 AUTHOR: Christman J W; Lancaster L H; Blackwell T S
 CORPORATE SOURCE: Department of Medicine, Vanderbilt University School of Medicine and the Department of Veterans Affairs, Nashville, TN 37322-2650, USA.. john.christman@mcmail.vanderbilt.edu
 CONTRACT NUMBER: HL 07123 (United States NHLBI)
 SOURCE: Intensive care medicine, (1998 Nov) Vol. 24, No. 11, pp. 1131-8. Ref: 81
 Journal code: 7704851. ISSN: 0342-4642.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 (RESEARCH SUPPORT, NON-U.S. GOV'T)
 (RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
 (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
 General Review; (REVIEW)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199903
 ENTRY DATE: Entered STN: 24 Mar 1999
 Last Updated on STN: 20 Apr 2002
 Entered Medline: 5 Mar 1999
 AB NF-kappaB is an important transcription factor complex that appears to play a fundamental role in regulating acute inflammation through activation of the cytokine cascade and production of other pro-inflammatory mediators. There is increasing evidence that NF-kappaB is important in the pathobiology of disease states such as SIRS, MODS and ARDS; therefore, therapeutic interventions aimed at limiting NF-kappaB activation and down-regulating production of inflammatory mediators could prove to be beneficial in decreasing host-derived tissue injury and organ dysfunction. Specific interventions that hold promise for suppressing NF-kappaB activation include the use of antioxidants, inhibition of NIK and the IKK signalsome, treatment with proteasome inhibitors, induction of endotoxin tolerance and, possibly the use of corticosteroids in selected patients.

L14 ANSWER 38 OF 76 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
 ACCESSION NUMBER: 2004:204238 BIOSIS
 DOCUMENT NUMBER: PREV200400204781
 TITLE: SIVA is upregulated in response to p53 mediated neuronal cell death.
 AUTHOR(S): Fortin, A. J.; Cregan, S. P.; Kushwaha, N.; Callaghan, S. M.; Thompson, C. [Reprint Author]; Park, D. S. [Reprint Author]; Slack, R. S. [Reprint Author]
 CORPORATE SOURCE: Neurosci., OHRI, Ottawa, ON, Canada
 SOURCE: Society for Neuroscience Abstract Viewer and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. 750.2.
<http://sfn.scholarone.com>. e-file.
 Meeting Info.: 33rd Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 08-12, 2003.

Society of Neuroscience.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

AB P53 has been implicated as a key regulator of neuronal cell death following acute injury. We have previously shown that p53-mediated neuronal cell death involves a Bax-dependent activation of caspase-3. It is believed that this process also requires de novo synthesis. P53 is a transcriptional activator and its targets in the regulation of neuronal apoptosis remain unknown. Recently, we have demonstrated that the direct transcriptional activation of Apaf1 by p53 is a critical step in the induction of neuronal cell death. To identify additional p53 targets, pro-apoptotic genes upregulated as per DNA microarray analysis using total RNA obtained from neurons following p53 expression have been identified. One of these, SIVA an adapter protein carrying a death domain, has consistently demonstrated a 4 fold increase in mRNA expression. It is thought to bind to CD27 a member of the TNFa receptor family and has been shown to induce apoptosis when expressed in various cell lines. Here we demonstrate that the expression of Siva in primary cultures of cerebellar granule neurons and neuronal precursor cells is sufficient to induce cell death. Our results also demonstrate SIVA upregulation following treatment with the DNA damaging agent camptothecin and following induction of focal ischemia by middle cerebral artery occlusion both believed to induce cell death in a p53-dependent manner. Analysis of a potential promoter region for human SIVA failed to uncover p53 consensus binding sequences, however, several E2F binding sites were identified. Interestingly, analysis of the mouse SIVA gene identified E2F binding sites within a putative promoter region and potential p53 consensus binding sites within intron1. Future studies will focus on examining the link between p53/E2F and SIVA upregulation and the mechanisms of SIVA induced apoptosis.

L14 ANSWER 40 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:445300 CAPLUS
DOCUMENT NUMBER: 148:417890
TITLE: TRAF2?TRAF3/p53 biomarkers and assays for the treatment of cancer with a lymphotoxin-β receptor activating agent
INVENTOR(S): Lukashev, Matvey E.; Bista, Pradeep; Zeng, Wei
PATENT ASSIGNEE(S): Biogen Idec Ma Inc., USA
SOURCE: PCT Int. Appl., 121pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2008042436	A2	20080410	WO 2007-US21356	20071003
WO 2008042436	A3	20081113		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,				

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-848956P P 20061003

AB The invention discloses methods for prognosticating the efficacy of a cancer treatment comprising administration of a lymphotoxin- β receptor activating agent, using TRAF3, TRAF2, and/or p53 markers, as well as combination therapies that include a composition that activates lymphotoxin- β receptor signaling in combination with one or more other agents.

L14 ANSWER 41 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:539218 CAPLUS
DOCUMENT NUMBER: 149:173578
TITLE: Immunotherapy for clinically isolated syndrome? Not necessarily...

AUTHOR(S): Siva, Aksel
CORPORATE SOURCE: Clinical Neuroimmunology Unit in the Neurology Department, Cerrahpasa School of Medicine, Istanbul University, Istanbul, Turk.

SOURCE: Nature Clinical Practice Neurology (2008), 4(5), 236-237

CODEN: NCPND4; ISSN: 1745-834X

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Multiple sclerosis (MS) is a complex disease with a high degree of clin. and neuropathol. variability between patients. In this Viewpoint, Aksel Siva argues that such a heterogeneous disease demands a heterogeneous approach to treatment and questions the practice of initiating long-term immunotherapy before the MS diagnosis has become definite.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 43 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2007:1361123 CAPLUS

DOCUMENT NUMBER: 148:4474

TITLE: Diagnostic agents and uses therefor

INVENTOR(S): Thomas, Ranjeny; Cardinal, John William; Mollah, Zia Uddin Ahmed

PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 86pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007134386	A1	20071129	WO 2007-AU692	20070518
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,			

GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: AU 2006-902684 A 20060518

AB The present invention discloses methods and agents for diagnosing the presence or risk of developing type 1 diabetes in animals, especially vertebrate animals. Also disclosed are novel surrogate markers for this disease including members of the nuclear factor κ B (NF- κ B) pathway. The present invention also extends to methods for treating or preventing type 1 diabetes, which employ the diagnostic method of the invention. The presence or risk of development of type 1 diabetes is diagnosed by detecting aberrant signaling through the NF- κ B pathway in response to a pro-inflammatory signal. NF- κ B expression was screened by immunoblotting cytoplasmic and nuclear exts. of dendritic cells generated in the presence of GM-CSF and IL-4 for 48 h from peripheral blood monocytes of type 1 diabetic patients and healthy controls. In nuclear exts., RelB, RelA, c-Rel, p52 and p50 increased in response to LPS in DC from healthy control but not from diabetic patients. Addnl., binding of nuclear RelB to DNA was reduced after 24 h of LPS exposure.

L14 ANSWER 52 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:293026 CAPLUS

DOCUMENT NUMBER: 144:338057

TITLE: Pharmaceuticals agents comprising blood components 10 kDa and their use for prophylaxis and treatment of defects of the immune system

INVENTOR(S): Salama, Zoser B.

PATENT ASSIGNEE(S): Germany

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1640012	A1	20060329	EP 2004-90376	20040924
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
AU 2005287727	A1	20060330	AU 2005-287727	20050926
CA 2580192	A1	20060330	CA 2005-2580192	20050926
WO 2006032269	A2	20060330	WO 2005-DE1729	20050926
WO 2006032269	A3	20060615		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1796695	A2	20070620	EP 2005-800702	20050926
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101060851	A	20071024	CN 2005-80032098	20050926
JP 2008514556	T	20080508	JP 2007-532768	20050926
BR 2005017349	A	20081007	BR 2005-17349	20050926

MX 200703489 A 20070518 MX 2007-3489 20070323
 US 20080220083 A1 20080911 US 2007-575931 20071108
 PRIORITY APPLN. INFO.: EP 2004-90376 A 20040924
 US 2004-948753 A 20040924
 WO 2005-DE1729 W 20050926

AB The invention relates to a composition consisting of proteins, peptides and/or peptide constituents, a pharmaceutical product containing said composition, a method for producing said composition, and the use thereof for the prophylaxis or therapy of people, animal and/or patients with pathogenic modifications and/or defects of cellular immunity, especially cancer, sepsis or allergic reactions, in conjunction with cytostatic therapy, chemotherapy and/or radiotherapy.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 53 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:1218470 CAPLUS
 DOCUMENT NUMBER: 143:452858
 TITLE: Use of a modulator of gene expression in the treatment of cancer
 INVENTOR(S): Rogers, Helen Louise; Willis, Anne; Bushell, Martin
 PATENT ASSIGNEE(S): The University of Nottingham, UK
 SOURCE: PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005107782	A2	20051117	WO 2005-GB1765	20050510
WO 2005107782	A3	20060202		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, VZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2004-10379 A 20040511

AB The use of a modulator of the activity of one or more genes, or a modulator of the activity of the expression product of one or more genes, wherein the one or more genes are selected from the group comprising cell surface receptor genes, genes associated with apoptosis, genes associated with cell proliferation and genes associated with cell cycle progression, in the treatment of cancer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 55 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:729611 CAPLUS
 DOCUMENT NUMBER: 143:206465
 TITLE: Therapeutic and carrier molecules
 INVENTOR(S): Ferrante, Antonio; Rathjen, Deborah Ann
 PATENT ASSIGNEE(S): Peplin Biolipids Pty Ltd, Australia
 SOURCE: PCT Int. Appl., 180 pp.

DOCUMENT TYPE: CODEN: PIXXD2
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: English
 PATENT INFORMATION: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005073164	A1	20050811	WO 2005-AU98	20050128
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005209331	A1	20050811	AU 2005-209331	20050128
CA 2554735	A1	20050811	CA 2005-2554735	20050128
EP 1718602	A1	20061108	EP 2005-700130	20050128
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			
CN 1934072	A	20070321	CN 2005-80008891	20050128
BR 2005007236	A	20070626	BR 2005-7236	20050128
JP 2007522118	T	20070809	JP 2006-549788	20050128
PRIORITY APPLN. INFO.:			US 2004-540604P	P 20040130
			WO 2005-AU98	W 20050128

OTHER SOURCE(S): MARPAT 143:206465

AB The present invention relates generally to compds. comprising a hydrocarbon chain portion and more particularly to compds. comprising chemical derivatizations of the hydrocarbon chain which are useful therapeutic and prophylactic mols. The present invention further provides compds. where the hydrocarbon chain portion is a carrier mol. for functional groups, moieties or agents. The present invention can include naturally including polyunsatd. fatty acids as well as synthetic, modified or derivatized polyunsatd. fatty acids. Furthermore, these polyunsatd. fatty acids can be conjugated to amino acids, peptides or proteins. The compds. of the present invention are particularly useful in the treatment and prophylaxis of a range of conditions including cancers, protein kinase c(PKC)- or NFkB-related- or -associated conditions, cardiovascular conditions, pain, inflammatory conditions, vascular or immunol. conditions such as diabetes, neurol. conditions and infection by a range of viruses or prokaryotic or eukaryotic organisms. The present invention further provides pharmaceutical compns. and methods of medical treatment.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 57 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:120930 CAPLUS

DOCUMENT NUMBER: 142:219282

TITLE: Pyrazoloisoquinoline derivatives as kinase inhibitors, and their preparation, pharmaceutical compositions, and use in the treatment of diseases involving increased NIK activity.

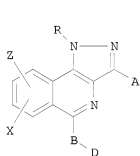
INVENTOR(S): Majid, Tahir N.; Hopkins, Corey; Pedgrift, Brian L.; Collar, Nicola; Wirtz-Brugger, Friederike; Merrill, Jean

PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA

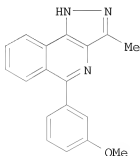
SOURCE: PCT Int. Appl., 94 pp.

DOCUMENT TYPE: CODEN: PIXXD2
 LANGUAGE: Patent
 FAMILY ACC. NUM. COUNT: 1 English
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012301	A1	20050210	WO 2003-US21144	20030703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, IJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2531291	A1	20050210	CA 2003-2531291	20030703
AU 2003304380	A1	20050215	AU 2003-304380	20030703
EP 1644371	A1	20060412	EP 2003-742433	20030703
EP 1644371	B1	20080213		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
CN 1802373	A	20060712	CN 2003-826733	20030703
BR 2003018383	A	20060725	BR 2003-18383	20030703
JP 2007521227	T	20070802	JP 2005-507449	20030703
AT 386034	T	20080315	AT 2003-742433	20030703
MX 2005PA13485	A	20060405	MX 2005-PA13485	20051213
KR 2006063872	A	20060612	KR 2006-700178	20060103
IN 2006CN00034	A	20070601	IN 2006-CN34	20060103
PRIORITY APPLN. INFO.:			WO 2003-US21144	W 20030703
OTHER SOURCE(S):	CASREACT 142:219282; MARPAT 142:219282			
GI				



I



II

AB Novel pyrazoloisoquinoline derivs. I, useful as kinase inhibitors, are disclosed [wherein: A = (un)substituted alkyl, OH or derivs., SH or derivs., CO₂H or derivs., NH₂ or derivs., cyano, (un)substituted heteroaryl, cycloalkyl, or heterocyclyl; B = bond, (un)substituted CH:CH, C.tplbond.C, O(CH₂)₁₋₄, O, S, CO, (un)substituted NH, NHC(O), CONH, NHSO₂, SO₂NH, NHC(O)NH, or C1-4 alkylene; D = (un)substituted alkyl, heteroaryl, heterocyclyl, aryl, or cycloalkyl; or BD = H, halo, fluoroalkoxy, (un)substituted alkyl; R = H, alkyl, (un)substituted arylalkyl; X, Z = H, alkyl, OH, alkoxy, halo, fluoroalkyl, CO₂H or derivs., NH₂ or derivs., cyano, SH or derivs., (un)substituted heterocyclyl or cycloalkyl; with provisos]. I are suitable for producing pharmaceuticals for the

prophylaxis and therapy of diseases whose course involves an increased activity of NIK. Approx. 75 examples were prepared, and these plus addnl. compds. are individually claimed. For instance, 3-methoxybenzoic acid was condensed with 3-methyl-5-phenyl-1H-pyrazol-4-ylamine using HOBT and DIPC, and the resultant benzamide derivative was cyclized by treatment with P2O5 and POC13 in xylene at 160°, to give title compound II. In a test for inhibition of release of IL1 β , TNF α , and IL6 in LPS-stimulated heparinized whole human blood, II had IC50 values of 1.3, 1.2, and 7 μ M, resp.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 58 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965429 CAPLUS

DOCUMENT NUMBER: 141:409384

TITLE: Gene expression profiles and methods for prognosis and treatment of solid tumors

INVENTOR(S): Strahs, Andrew; Trepicchio, William L.; Burczynski, Michael E.; Twine, Natalie C.; Slonim, Donna K.; Immerman, Fred; Dorner, Andrew J.

PATENT ASSIGNEE(S): Wyeth, John and Brother Ltd., USA

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004097052	A2	20041111	WO 2004-US13587	20040429
WO 2004097052	A3	20050414		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EG, ES, FI, GB, GD, GE, GH, GM, GR, GU, HK, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TG, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2004235395	A1	20041111	AU 2004-235395	20040429
CA 2523798	A1	20041111	CA 2004-2523798	20040429
EP 1618218	A2	20060125	EP 2004-760461	20040429
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR			
US 20060194211	A1	20060831	US 2004-834268	20040429
US 20080032299	A1	20080207	US 2007-715606	20070308
PRIORITY APPLN. INFO.:			US 2003-466067P	P 20030429
			US 2004-538246P	P 20040123
			US 2004-834268	B1 20040429
			WO 2004-US13587	W 20040429
AB	Solid tumor prognosis genes, and methods, systems, and equipment of using these genes for the prognosis and treatment of solid tumors are provided. Gene expression profiles in peripheral blood mononuclear cells (PBMCs) of patients with renal cell carcinoma are determined prior to and after CCI-779 therapy using the Affymetrix HgU95A genechips. Of the 12,626 genes on the HgU95A chip, 5424 genes met the initial criteria (i.e., at least one present call across the data set and at least one frequency \geq 10 ppm). On the basis of Spearman's rank correlation, Cox proportional			

hazard modeling, Motzer risk classification, hierarchical clustering, and k-nearest-neighbors or weighted voting algorithm, subsets of genes are provided whose expression in PBMCS are pos. or neg. correlated with clin. outcome of the solid tumor. The prognosis genes of the present invention can be used as surrogate markers for predicting clin. outcome of a solid tumor in a patient of interest. These genes can also be used to select a treatment which has a favorable prognosis for the solid tumor of the patient of interest.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 61 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:41469 CAPLUS

DOCUMENT NUMBER: 140:94041

TITLE: Preparation of pyrazoloisoquinolines as NF

κB-inducing kinase (NIK) inhibitors

INVENTOR(S): Flohr, Stefanie; Naumann, Thorsten

PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

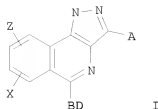
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004005287	A1	20040115	WO 2003-EP6500	20030620
WO 2004005287	A9	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10229762	A1	20040122	DE 2002-10229762	20020703
CA 2490571	A1	20040115	CA 2003-2490571	20030620
AU 2003242737	A1	20040123	AU 2003-242737	20030620
EP 1519934	A1	20050406	EP 2003-762498	20030620
EP 1519934	B1	20070919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003012424	A	20050426	BR 2003-12424	20030620
JP 2006513137	T	20060420	JP 2004-518545	20030620
AT 373658	T	20071015	AT 2003-762498	20030620
US 20040097541	A1	20040520	US 2003-613482	20030703
US 6841556	B2	20050111		
MX 2005PA00038	A	20050408	MX 2005-PA38	20050103
PRIORITY APPLN. INFO.:			DE 2002-10229762	A 20020703
			US 2002-423954P	P 20021105
			WO 2003-EP6500	W 20030620

OTHER SOURCE(S): MARPAT 140:94041

GI



AB Title compds. [I; A = alkyl substituted by 1-2 OR1, CO2R1, (substituted) heteroaryl; B = bond, R1-substituted alkylene; D = (substituted) heteroaryl, heterocyclyl, aryl, cycloalkyl; X, Y = H, alkyl, OH, alkoxy, halo; R1 = H, alkyl], were prepared. Thus, PhCO2H, hydroxybenzotriazole, diisopropyl carbodiimide, and 3,5-diphenyl-1H-pyrazol-4-ylamine were stirred 12 h in MeCN to give a residue which was heated with P2O5 and POC13 in xylene at 150° for 4 h and at room temperature for 12 h to give 3,5-diphenyl-1H-pyrazolo[4,3-c]isoquinoline. The latter inhibited TNF α release in LPS-stimulated human peripheral blood lymphocytes with IC50 = 1.9 μ M.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 70 OF 76 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1997:698007 CAPLUS

DOCUMENT NUMBER: 128:46315

ORIGINAL REFERENCE NO.: 128:9059a,9062a

TITLE: I κ B kinase- β : NF- κ B activation and complex formation with I κ B kinase- α and NIK

AUTHOR(S): Woronicz, John D.; Gao, Xiong; Cao, Zhaodan; Rothe, Mike; Goeddel, David V.

CORPORATE SOURCE: Tularik, South San Francisco, CA, 94080, USA

SOURCE: Science (Washington, D. C.) (1997), 278(5339), 866-869
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Activation of the transcription factor nuclear factor kappa B (NF- κ B) by inflammatory cytokines requires the successive action of NF- κ B-inducing kinase (NIK) and I κ B kinase- α (IKK- α). A widely expressed protein kinase was identified that is 52 % identical to IKK- α . I κ B kinase- β (IKK- β) activated NF- κ B when overexpressed and phosphorylated serine residues 32 and 36 of I κ B- α and serines 19 and 23 of I κ B- β . The activity of IKK- β was stimulated by tumor necrosis factor and interleukin-1 treatment. IKK- α and IKK- β formed heterodimers that interacted with NIK. Overexpression of a catalytically inactive form of IKK- β blocked cytokine-induced NF- κ B activation. Thus, an active I κ B kinase complex may require three distinct protein kinases.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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STN INTERNATIONAL SESSION SUSPENDED AT 16:49:29 ON 06 JAN 2009

Connecting via Winsock to STN

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PASSWORD:

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AT 17:07:34 ON 06 JAN 2009
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FILE 'BIOSIS' ENTERED AT 17:07:34 ON 06 JAN 2009
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FILE 'CAPLUS' ENTERED AT 17:07:34 ON 06 JAN 2009
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FILE 'EMBASE' ENTERED AT 17:07:34 ON 06 JAN 2009
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	ENTRY	SESSION
FULL ESTIMATED COST	218.88	219.10
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-9.02	-9.02

=> S (siRNA OR RNAi) (S) treatment(S) leukemia AND 20041130
L15 0 (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND 20041130

=> S (siRNA OR RNAi) (S) treatment(S) leukemia AND pd<=20041130
1 FILES SEARCHED...
L16 15 (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND PD<=20041130

=> Dup REM L15
L15 HAS NO ANSWERS

=> Dup Rem l16
PROCESSING COMPLETED FOR L16
L17 10 DUP REM L16 (5 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWER '3' FROM FILE BIOSIS
ANSWERS '4-10' FROM FILE CAPLUS

=> D TI L16 1-10

L16 ANSWER 1 OF 15 MEDLINE on STN
TI Reversal of P-glycoprotein-mediated multidrug resistance with small
interference RNA (siRNA) in leukemia cells.

L16 ANSWER 2 OF 15 MEDLINE on STN
TI Targeting oncogenic fusion genes in leukemias and lymphomas by RNA
interference.

L16 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
TI Reversal of P-glycoprotein-mediated multidrug resistance with small
interference RNA (siRNA) in leukemia cells.

L16 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
TI Reversal of P-glycoprotein-mediated multidrug resistance by small
interference RNA (siRNA) in leukemia cells.

L16 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Compositions and methods involving cancer-associated gene expression for treatment and diagnosis of lymphoma and leukemia

L16 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Viral vectors for siRNA-mediated gene silencing of huntingtin or ataxin-1 for treatment of neurodegenerative diseases

L16 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Reversal of P-glycoprotein-mediated multidrug resistance with small interference RNA (siRNA) in leukemia cells

L16 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI siRNA targeting human CD40 mRNA for use in disease treatment

L16 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI siRNA targeting inhibitor of apoptosis protein livin for treatment of therapy-resistant tumors

L16 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 TI Double-stranded RNA for RNAi and treatment of disease

=> D Ibib abs L16 5,8,9,10

L16 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2007:488659 CAPLUS
 DOCUMENT NUMBER: 146:475660
 TITLE: Compositions and methods involving cancer-associated gene expression for treatment and diagnosis of lymphoma and leukemia
 INVENTOR(S): Pedersen, Finn Skou; Sorensen, Annette Balle; Hernandez, Javier Martin; Nielsen, Anne Ahlmann; Moving, Helle
 PATENT ASSIGNEE(S): Den.
 SOURCE: U.S. Pat. Appl. Publ., 44pp., Cont.-in-part of U.S. Ser. No. 365,889.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 12
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20070098728	A1	20070503	US 2006-438734	20060522
US 20020115058	A1	20020822	US 2001-962929	20010924 <--
US 20020164576	A1	20021107	US 2001-962855	20010924 <--
US 20030044803	A1	20030306	US 2001-962854	20010924 <--
US 20030077590	A1	20030424	US 2001-962916	20010924 <--
US 20030224460	A1	20031204	US 2001-963131	20010924 <--
US 20070059724	A1	20070315	US 2006-365889	20060301
AU 2008201683	A1	20080508	AU 2008-201683	20080416
PRIORITY APPLN. INFO.:				
			US 2001-962854	A2 20010924
			US 2001-962855	A2 20010924
			US 2001-962916	A2 20010924
			US 2001-962929	A2 20010924
			US 2001-963131	A3 20010924
			US 2006-365889	A2 20060301
			US 2000-668644	A2 20000922
			US 2001-905390	B2 20010713

US 2001-905491 B2 20010713
 AU 2002-328896 A3 20020715

AB This invention is in the field of cancer-associated (CA) genes. Specifically it relates to methods for detecting and diagnosing cancer or the likelihood of developing cancer based on the presence or absence of expression of PI3KR1, GNAS, NESP5, JAK1, neurogranin, HIPK1, or Nrf2, or proteins encoded by those genes. The invention also provides antibodies, antisense nucleic acids, and siRNA's for upregulating or downregulating these cancer-associated genes and methods for treatment of lymphoma and leukemia.

L16 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2009 ACS ON STN

ACCESSION NUMBER: 2004:878487 CAPLUS

DOCUMENT NUMBER: 141:343481

TITLE: SiRNA targeting human CD40 mRNA for use in disease treatment

INVENTOR(S): Aran Perramon, Josep Maria; Grinyo Boira, Josep Maria; Torras Ambros, Juan; Pluvinet Ortega, Raquel; Cruzado Garrit, Josep Maria; Herrero Fresneda, Immaculada Spain

PATENT ASSIGNEE(S): PCT Int. Appl., 52 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Spanish

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090134	A1	20041021	WO 2004-ES117	20040315 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2216707	A1	20041016	ES 2003-822	20030408 <--
ES 2216707	B1	20051216		
EP 1614751	A1	20060111	EP 2004-720630	20040315
EP 1614751	B1	20070516		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
AT 362537	T	20070615	AT 2004-720630	20040315
PRIORITY APPLN. INFO.:			ES 2003-822	A 20030408
			WO 2004-ES117	W 20040315

AB The invention relates to oligoribonucleotide sequences 5'-ggcaauccuagacaccug-3' and 5'-caggugcuaggaaucgc-3' which are homologous to the region between nucleotides 241 and 259 in the cDNA which codes for the human CD40 receptor, as found in the GeneBank accession number X60592, as well as sequences and duplex oligonucleotides derived therefrom. The invention also refers to pharmaceutical compns. comprising them, to vectors encoding these siRNAs, and their use in disease treatment, e.g., for inhibiting the expression of the human CD40 receptor, for blocking or reducing the interaction between human CD40 and CD40L, etc..

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:876013 CAPLUS
 DOCUMENT NUMBER: 141:343471
 TITLE: SiRNA targeting inhibitor of apoptosis protein livin
 for treatment of therapy-resistant tumors
 INVENTOR(S): Butz, Karin; Crnkovic-Mertens, Irena; Hoppe-Seyler,
 Felix
 PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung Des
 Oeffentlichen Rechts, Germany
 SOURCE: Eur. Pat. Appl., 22 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1469070	A1	20041020	EP 2003-8081	20030415 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
WO 2004091388	A1	20041028	WO 2004-EP3974	20040415 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20060264394	A1	20061123	US 2006-553355	20060705
PRIORITY APPLN. INFO.:			EP 2003-8081 A 20030415 WO 2004-EP3974 W 20040415	
AB Provided is the use of siRNAs which are specific for the inhibitor of apoptosis protein (IAP) livin-1 and Livin-2 to sensitize tumor cells for apoptosis by down-regulating livin expression. The invention also provides the vector pSUPER for production of the siRNAs. Livin-2 siRNA increased caspase-3-like activities and enhanced apoptosis in livin-pos. cells treated with pro-apoptotic stimuli.				
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L16 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2004:143294 CAPLUS
 DOCUMENT NUMBER: 140:194397
 TITLE: Double-stranded RNA for RNAi and treatment of disease
 INVENTOR(S): Giese, Klaus; Kaufmann, Joerg; Klippel-Giese, Anke
 PATENT ASSIGNEE(S): Atugen Ag, Germany
 SOURCE: PCT Int. Appl., 150 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004015107	A2	20040219	WO 2003-EP8666	20030805 <--

WO 2004015107 A3 20040429

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1389637 A1 20040218 EP 2002-17601 20020805 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

CA 2494930 A1 20040219 CA 2003-2494930 20030805 <--

AU 2003260370 A1 20040225 AU 2003-260370 20030805 <--

AU 2003260370 B2 20080522

EP 1527176 A2 20050504 EP 2003-784183 20030805

EP 1527176 B1 20070103

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003013202 A 20050621 BR 2003-13202 20030805

CN 1675359 A 20050928 CN 2003-818867 20030805

JP 2006500014 T 20060105 JP 2004-526885 20030805

MX 2005PA01355 A 20050930 MX 2005-PA1355 20050202

IN 2005DN00427 A 20081128 IN 2005-DN427 20050203

IN 2007DN06736 A 20070921 IN 2007-DN6736 20070830

AU 2008207337 A1 20080904 AU 2008-207337 20080815

PRIORITY APPLN. INFO.: EP 2002-17601 A 20020805

US 2002-402541P P 20020812

EP 2003-8383 A 20030410

AU 2003-260370 A3 20030805

WO 2003-EP8666 W 20030805

IN 2005-DN427 A3 20050203

AB Double-stranded RNA (dsRNA) for inhibition of gene expression by RNA interference is disclosed. The dsRNA may be blunt-ended, some of the termini may be modified, and one or both strands may contain modified nucleosides, e.g., 2'-O-methylribonucleosides. The optimal length is 18-19 nucleotides. The dsRNA may be used to treat various diseases, e.g., cancer, diabetes, cardiovascular disease, etc. Thus, extensive experimentation indicated that there is no need of overlapping ends, that modification of the ends of the sense strand enhances the activity, and that inclusion of modified nucleosides enhances nuclease resistance but decreases inhibition unless placement of the modified nucleosides is optimized. For example, alteration of 2'-O-methylribosides with unmodified residues provides nuclease resistance but does not interfere with inhibitory activity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> Log Off h

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 17:12:40 ON 06 JAN 2009

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

LOGINID/PASSWORD REJECTED

The loginid and/or password sent to STN were invalid.
You either typed them incorrectly, or line noise may
have corrupted them.

Do you wish to retry the logon?

Enter choice (y/N):

Do you wish to use the same loginid and password?

Enter choice (y/N):

Enter new loginid (or press [Enter] for SSPTAEGS1646):

Enter new password:

LOGINID:LOGINID: SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
AT 17:17:05 ON 06 JAN 2009
FILE 'MEDLINE' ENTERED AT 17:17:05 ON 06 JAN 2009
FILE 'BIOSIS' ENTERED AT 17:17:05 ON 06 JAN 2009
Copyright (c) 2009 The Thomson Corporation
FILE 'CAPLUS' ENTERED AT 17:17:05 ON 06 JAN 2009
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)
FILE 'EMBASE' ENTERED AT 17:17:05 ON 06 JAN 2009
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	261.91	262.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.30	-12.30

=> D hist

(FILE 'HOME' ENTERED AT 15:51:25 ON 06 JAN 2009)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:51:58 ON 06 JAN 2009

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L1      0 S (NIK OR SIVA) (S) MODULAT? (S) (IMMUNE(6A)DISORDER) AND PD<=2
L2      0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L3      0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L4      0 S (NIK(S)SIVA) (S) COMPLEX AND PD<=20041130
L5      0 S (NIK(S)SIVA) (S) BINDING AND PD<=20041130
L6      0 S (NIK (S) SIVA) (S) BINDING AND PD<=20041130
L7      1 S (NIK(S)SIVA) (S) BINDING
L8      0 S (NIK (S) SIVA) (S) INTERACTION AND PD<=20041130
L9      0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA AND PD<=20041130
L10     0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA
L11     157 S (NIK OR SIVA) (S) TREATMENT
L12     0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER) AND PD<=200
L13     0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER)
L14     76 DUP REM L11 (81 DUPLICATES REMOVED)
L15     0 S (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND 20041130
L16     15 S (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND PD<=20041130
L17     10 DUP REM L16 (5 DUPLICATES REMOVED)
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=> S (shRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA

L18 11 (SHRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA

=> Dup rem L18

PROCESSING COMPLETED FOR L18

L19 9 DUP REM L18 (2 DUPLICATES REMOVED)

ANSWER '1' FROM FILE MEDLINE

ANSWERS '2-9' FROM FILE CAPLUS

=> D ti L19 1-9

L19 ANSWER 1 OF 9 MEDLINE on STN DUPLICATE 1

TI Targeting oncogenic fusion genes in leukemias and lymphomas by RNA interference.

L19 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Pharmaceutical combinations of staurosporines with antisense oligonucleotides or mcl-1-specific RNAi constructs, for treatment of myelodysplastic syndromes, lymphomas, leukemias, and solid tumors

L19 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Expressing multiple siRNAs and shRNAs from a single vector for tumor and infection therapy

L19 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Progress of RNAi in leukemia gene treatment

L19 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Identification of genes modulating signal transduction by the JAK/STAT pathway by genome-wide RNAi screening

L19 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI siRNA's and RNAi modulation of MLL-AF4 gene for treatment of proliferative disorders

L19 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI RNA interference-mediated silencing of synuclein gene expression and treatment of neurodegenerative diseases

L19 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Targeting primary human leukaemia cells with RNA interference: Bcr-Abl targeting inhibits myeloid progenitor self-renewal in chronic myeloid leukaemia cells

L19 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

TI Double-stranded RNA for RNAi and treatment of disease

=> Log off h

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 17:20:18 ON 06 JAN 2009

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
 SESSION RESUMED IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE'
 AT 17:23:57 ON 06 JAN 2009
 FILE 'MEDLINE' ENTERED AT 17:23:57 ON 06 JAN 2009
 FILE 'BIOSIS' ENTERED AT 17:23:57 ON 06 JAN 2009
 Copyright (c) 2009 The Thomson Corporation
 FILE 'CAPLUS' ENTERED AT 17:23:57 ON 06 JAN 2009
 COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)
 FILE 'EMBASE' ENTERED AT 17:23:57 ON 06 JAN 2009
 Copyright (c) 2009 Elsevier B.V. All rights reserved.

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	277.58	277.80
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-12.30	-12.30

=> D hist

(FILE 'HOME' ENTERED AT 15:51:25 ON 06 JAN 2009)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:51:58 ON 06 JAN 2009

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L1      0 S (NIK OR SIVA) (S) MODULAT? (S) (IMMUNE(6A)DISORDER) AND PD<=2
L2      0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L3      0 S (NIK(S)SIVA) (S) COMPLEX (S) (IMMUNE? OR LEUKEMIA) AND PD<=20
L4      0 S (NIK(S)SIVA) (S) COMPLEX AND PD<=20041130
L5      0 S (NIK(S)SIVA) (S) BINDING AND PD<=20041130
L6      0 S (NIK (S) SIVA) (S) BINDING AND PD<=20041130
L7      1 S (NIK(S)SIVA) (S) BINDING
L8      0 S (NIK (S) SIVA) (S) INTERACTION AND PD<=20041130
L9      0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA AND PD<=20041130
L10     0 S (NIK OR SIVA) (S) TREATMENT (S) LEUKEMIA
L11     157 S (NIK OR SIVA) (S) TREATMENT
L12     0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER) AND PD<=200
L13     0 S (NIK OR SIVA) (S) TREATMENT (P) (IMMUNE DISORDER)
L14     76 DUP REM L11 (81 DUPLICATES REMOVED)
L15     0 S (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND 20041130
L16     15 S (SIRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA AND PD<=20041130
L17     10 DUP REM L16 (5 DUPLICATES REMOVED)
L18     11 S (SHRNA OR RNAI) (S) TREATMENT(S) LEUKEMIA
L19     9 DUP REM L18 (2 DUPLICATES REMOVED)
  
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=> D ibib abs L19 2,4,7-9

L19 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2009 ACS ON STN
 ACCESSION NUMBER: 2007:1468876 CAPLUS
 DOCUMENT NUMBER: 148:106169
 TITLE: Pharmaceutical combinations of staurosporines with
 antisense oligonucleotides or mcl-1-specific
 RNAi constructs, for treatment of
 myelodysplastic syndromes, lymphomas,
 leukemias, and solid tumors
 INVENTOR(S): Valent, Peter
 PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
 SOURCE: PCT Int. Appl., 65pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007/147613	A2	20071227	WO 2007-EP5517	20070622
WO 2007/147613	A3	20080703		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRIORITY APPLN. INFO.: GB 2006-12542 A 20060623

OTHER SOURCE(S): MARPAT 148:106169

AB The present invention relates to a method of treating myelodysplastic syndromes, lymphomas and leukemias, and also solid tumors with a pharmaceutical combination of a FLT-3 kinase inhibitor and an antisense oligonucleotide or a mcl-1 -specific RNAi construct. It also relates to the use of a pharmaceutical combination of a histone deacetylase inhibitor and a FLT-3 kinase inhibitor for the treatment of the diseases or malignancies mentioned above and the use of such a pharmaceutical composition for the manufacture of a medicament for the treatment of these diseases or malignancies. Thus, patients with systemic mastocytosis were examined and subjected to biopsy; human mast cell line HMC-1 generated from leukemic cells was obtained. HMC-1 cells were incubated with tyrosine kinase (TK) inhibitor PKC412 (100 pM through 10 μM), nilotinib (1 nM through 100 μM), imatinib (3 nM through 300 μM), or 2CdA (0.1 - 10,000 ng/mL) for up to 48 h; in a sep. set of expts., HMC-1 cells were transfected with mcl-1-specific antisense oligonucleotide (ASO) before being exposed to the inhibitory drugs; in other expts., cells were transfected with various concns. of mcl-1-specific ASO (50 nM - 250 nM) for up to 12 h or with siRNA (200 nM) for 12 h without further exposure to targeted drugs. Our data showed that neoplastic mast cells (MC) express mcl-1, and that targeting of mcl-1 is associated with decreased survival and increased responsiveness against TK inhibitors such as PKC412. These data suggest that mcl-1 is a novel interesting target in neoplastic MC that may help to overcome resistance against TK inhibitors.

L19 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2008:783967 CAPLUS

TITLE: Progress of RNAi in leukemia gene treatment

AUTHOR(S): Tian, Caixia; Wang, Hongwei

CORPORATE SOURCE: Examine Institute of Hematology, The Second Hospital, Shanxi Medical University, Taiyuan, 030001, Peop. Rep. China

SOURCE: Zhongliu Yanjiu Yu Linchuang (2007), 19(4), 280-282
CODEN: ZYLIFJ; ISSN: 1006-9801

PUBLISHER: Zhongliu Yanjiu Yu Linchuang Zazhi Bianjibu

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB RNAi is double-strands RNA inhibiting specially target gene's expression and leads to post-transcript gene silence. SiRNA treatment targeted leukemia's fuse gene and Wt1 gene which leukemia express universally. SiRNA treatment is a effective method for leukemia gene treatment. However, RNAi has lots of problems waiting for solution when it is used in clinic.

L19 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2006:343958 CAPLUS
 DOCUMENT NUMBER: 144:383394
 TITLE: RNA interference-mediated silencing of synuclein gene expression and treatment of neurodegenerative diseases
 INVENTOR(S): Bohn, Martha C.; Sapru, Mohan
 PATENT ASSIGNEE(S): Children's Memorial Hospital, USA
 SOURCE: PCT Int. Appl., 60 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006039253	A2	20060413	WO 2005-US34516	20050927
WO 2006039253	A3	20061123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TG, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM CA 2580189 A1 20060413 CA 2005-2580189 20050927 EP 1799826 A2 20070627 EP 2005-816006 20050927 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU US 20070172462 A1 20070726 US 2007-726211 20070321 PRIORITY APPLN. INFO.: US 2004-614112P P 20040929 WO 2005-US34516 W 20050927				
AB The present invention is directed to siRNAs and shRNAs that downregulate expression of a synuclein gene and use of these siRNA/shRNA mols. to treat neurodegenerative diseases. Thus, α -synuclein mRNA-targeting shRNA silenced α -synuclein gene expression in the striatum upon injection into rat brain. Similar results were observed using siRNA in HeLa cell culture.				
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L19 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 2005:531465 CAPLUS
 DOCUMENT NUMBER: 143:126096
 TITLE: Targeting primary human leukaemia cells with RNA interference: Bcr-Abl targeting inhibits myeloid progenitor self-renewal in chronic myeloid leukaemia cells
 AUTHOR(S): Withey, Jane M. E.; Marley, Stephen B.; Kaeda, Jaspal; Harvey, Amanda J.; Crampton, Mark R.; Gordon, Myrtle Y.
 CORPORATE SOURCE: Department of Biomedical Sciences, School of Biological Sciences, Royal Holloway University of London, Surrey, UK
 SOURCE: British Journal of Haematology (2005), 129(3), 377-380

PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have investigated functional outcome of challenging primary chronic myeloid leukemia (CML) cells with Bcr-Abl fusion sequence-directed RNA interference (RNAi). We targeted the Bcr-Abl b3a2 variant, by RNAi, in primary chronic phase CML cells, and detected strikingly reduced proliferation of myeloid precursor cells expressing this variant. Lack of an effect in cells expressing a distinct Bcr-Abl variant confirmed the specificity of the response. Through the functional targeting of an oncogene in primary human tumor cells, we have demonstrated that Bcr-Abl enhances CML progenitor cell amplification, and that RNAi may be suitable for development as a specific anti-leukemia treatment.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:143294 CAPLUS
DOCUMENT NUMBER: 140:194397
TITLE: Double-stranded RNA for RNAi and treatment of disease
INVENTOR(S): Giese, Klaus; Kaufmann, Joerg; Klippel-Giese, Anke
PATENT ASSIGNEE(S): Atugen Ag, Germany
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004015107	A2	20040219	WO 2003-EP8666	20030805
WO 2004015107	A3	20040429		
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW:				
GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1389637	A1	20040218	EP 2002-17601	20020805
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2494930	A1	20040219	CA 2003-2494930	20030805
AU 2003260370	A1	20040225	AU 2003-260370	20030805
AU 2003260370	B2	20080522		
EP 1527176	A2	20050504	EP 2003-784183	20030805
EP 1527176	B1	20070103		
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013202	A	20050621	BR 2003-13202	20030805
CN 1675359	A	20050928	CN 2003-818867	20030805
JP 2006500014	T	20060105	JP 2004-526885	20030805
MX 2005PA01355	A	20050930	MX 2005-PA1355	20050202
IN 2005DN00427	A	20081128	IN 2005-DN427	20050203
IN 2007DN06736	A	20070921	IN 2007-DN6736	20070830
AU 2008207337	A1	20080904	AU 2008-207337	20080815

PRIORITY APPLN. INFO.:	EP 2002-17601	A	20020805
	US 2002-402541P	P	20020812
	EP 2003-8383	A	20030410
	AU 2003-260370	A3	20030805
	WO 2003-EP8666	W	20030805
	IN 2005-DN427	A3	20050203

AB Double-stranded RNA (dsRNA) for inhibition of gene expression by RNA interference is disclosed. The dsRNA may be blunt-ended, some of the termini may be modified, and one or both strands may contain modified nucleosides, e.g., 2'-O-methylribonucleosides. The optimal length is 18-19 nucleotides. The dsRNA may be used to treat various diseases, e.g., cancer, diabetes, cardiovascular disease, etc. Thus, extensive experimentation indicated that there is no need of overlapping ends, that modification of the ends of the sense strand enhances the activity, and that inclusion of modified nucleosides enhances nuclease resistance but decreases inhibition unless placement of the modified nucleosides is optimized. For example, alteration of 2'-O-methylribosides with unmodified residues provides nuclease resistance but does not interfere with inhibitory activity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS 5	OCT 22	Current-awareness alert (SDI) setup and editing enhanced
NEWS 6	OCT 22	WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 7	OCT 24	CHEMLIST enhanced with intermediate list of pre-registered REACH substances
NEWS 8	NOV 21	CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 9	NOV 26	MARPAT enhanced with FSORT command
NEWS 10	NOV 26	MEDLINE year-end processing temporarily halts availability of new fully-indexed citations
NEWS 11	NOV 26	CHEMSAFE now available on STN Easy
NEWS 12	NOV 26	Two new SET commands increase convenience of STN searching

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 NEWS 14 DEC 12 GBFULL now offers single source for full-text
 coverage of complete UK patent families
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 will change in 2009 for STN-Columbus and STN-Tokyo

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
 AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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=> S (Gene therapy) (S) (leukemia OR Lymphoma)
 L1 1886 (GENE THERAPY) (S) (LEUKEMIA OR LYMPHOMA)

=> L1 AND review
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=> S L1 AND review
 L2 267 L1 AND REVIEW

=> S L2 AND B-CLL
 L3 3 L2 AND B-CLL

=> Dup removal L3
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'REMOVAL' IS NOT VALID. VALID FILE NAMES ARE 'CAPLUS'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> Dup Rem L3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)
ANSWERS '1-3' FROM FILE CAPLUS

=> D ibib abs L3 1-3

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:317031 CAPLUS
DOCUMENT NUMBER: 141:172382
TITLE: The Potential of Gene Transfer into Primary B
-CLL Cells Using Recombinant Virus Vectors
AUTHOR(S): Wendtner, C-M.; Kofler, Dm; Mayr, C.; Bund, D.;
Hallek, M.
CORPORATE SOURCE: Medical Clinic III, Klinikum Grosshadern Medical
Center (KGMC), Munich, Germany
SOURCE: Leukemia & Lymphoma (2004), 45(5), 897-904
CODEN: LELYEA; ISSN: 1042-8194
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Despite recent advances, chronic lymphocytic leukemia
(CLL) as the most common leukemia remains a largely incurable disease.
Modern treatment options include novel drugs like purine analogs,
monoclonal antibodies and transplantation strategies. Moreover, gene
transfer of immunostimulatory mols. is another, but still exptl. approach
that can be used to potentiate immune responses against leukemic cells.
CD40 ligand (CD40L) was shown to be a promising mol. for immunotherapy of
B-CLL playing a critical role in immune activation.
However, CLL B cells are resistant to transduction with most currently
available vector systems. Improving the efficiency and specificity of
gene vectors is critical for the success of gene therapy in this area. Using
replication defective adenovirus encoding CD40L (Ad-CD40L), immunol. and
clin. responses were seen in CLL patients after infusion of autologous
Ad-CD40L-CLL cells in a recent phase I trial. Due to the immunogenic
nature of adenovirus vectors, alternative vector systems are currently
explored. Recombinant adeno-associated virus (rAAV) was shown to enable
efficient transduction of primary B-CLL cells. By use
of a library of AAV clones with randomly modified capsids,
receptor-targeting mutants with a tropism for CLL cells can be selected.
Furthermore, helper-virus free Epstein-Barr virus (EBV)-based gene
transfer vectors hold promise for development of CLL-targeted vaccines
after remaining safety issues will be resolved. Herpes simplex virus
(HSV)-based vectors, especially HSV amplicons, have favorable features for
B-CLL gene transfer including high transduction
efficiency, ability to infect postmitotic cells and a large packaging
capacity. The challenge for the future will be to transfer these
alternative vector systems into clinic and allow the detection of a
CLL-specific immune response by use of defined tumor antigens. This will
make it possible to establish the potential clin. role of gene therapy for
CLL patients.
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:910055 CAPLUS

DOCUMENT NUMBER: 135:151176
 TITLE: Immuno gene therapy of leukemia
 AUTHOR(S): Kato, Kazunori
 CORPORATE SOURCE: Dept. of Pharmacology, National Cancer Center, Japan
 SOURCE: Igaku no Ayumi (2000), 195(1), 43-49
 CODEN: IGAYAY; ISSN: 0039-2359
 PUBLISHER: Ishiyaku Shuppan
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese

AB A review with 7 refs. on CD40 ligand gene therapy of chronic lymphocytic leukemia. Topics included are gene therapy of malignant lymphoma/leukemia, chronic lymphocytic leukemia, acquired CD40 ligand deficiency in B-cell chronic lymphocytic leukemia (B-CLL), gene transfer of CD40 ligand, transformation of B-CLL to express CD40 ligand, and induction of autologous T cell activation by CD40 ligand transformed B-CLL. Clin. trial of CD40 ligand gene therapy of B-CLL using adenovirus vector is also discussed.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:873641 CAPLUS
 DOCUMENT NUMBER: 135:44805
 TITLE: Immuno gene therapy by CD40 ligand
 AUTHOR(S): Kato, Kazunori
 CORPORATE SOURCE: Pharmacology Division, National Cancer Center Research Institute, Japan
 SOURCE: Igaku no Ayumi (2000), 194(14), 1261-1266
 CODEN: IGAYAY; ISSN: 0039-2359
 PUBLISHER: Ishiyaku Shuppan
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: Japanese

AB A review with 21 refs. discussing gene therapy with CD40 ligand against chronic lymphocytic leukemia (CLL). Topics discussed include CD40 ligand mol., characteristics of B-chronic lymphocytic leukemia (B-CLL), expression of CD40 ligand in B-CLL, B-CLL cells transfected with CD40 ligand, and CD40 ligand gene therapy including administration, results, and anti-leukemia immune responses. Application to other tumors is also discussed.

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